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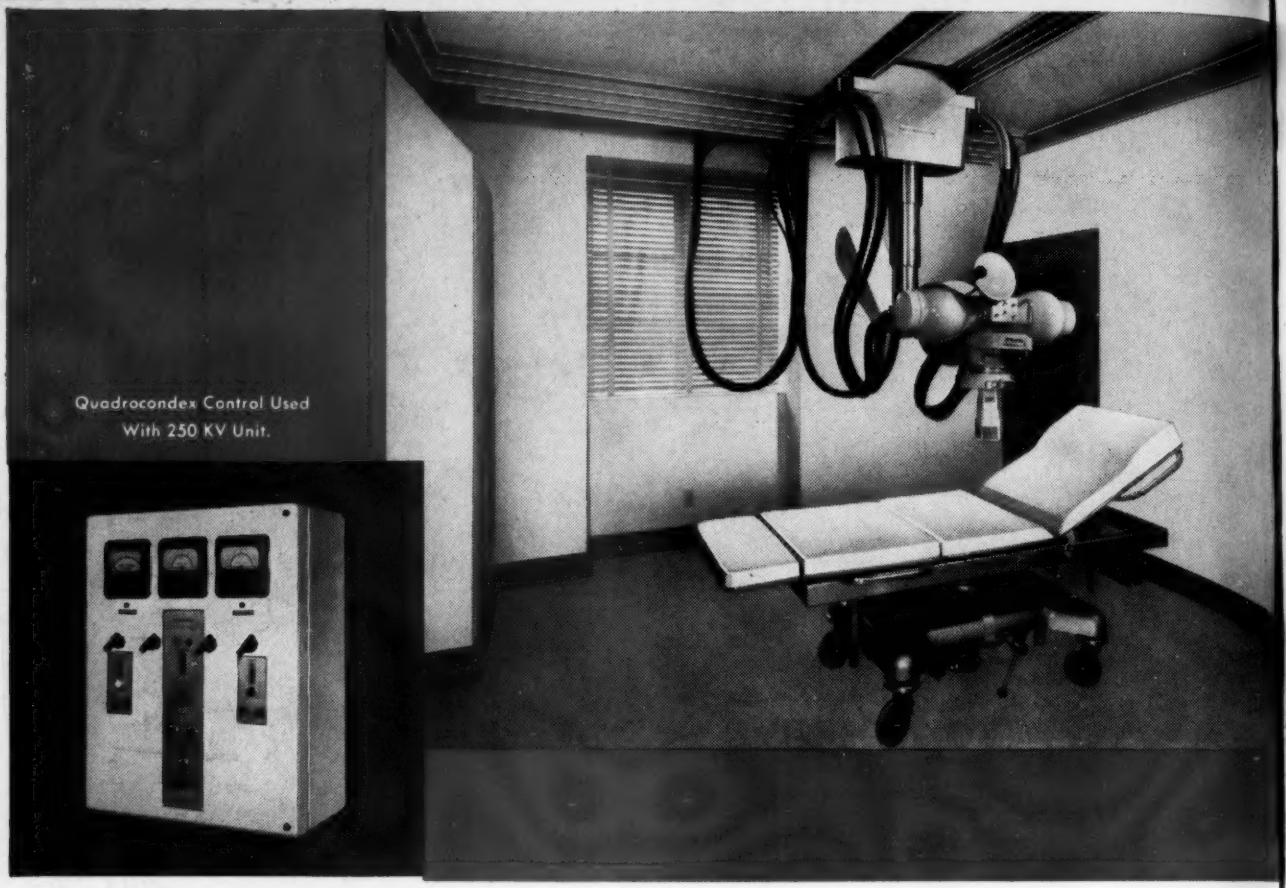

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THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 73 MAY, 1955 No. 5

CONGENITAL DUODENAL OBSTRUCTION

A CLINICAL, ROENTGENOLOGICAL, SURGICAL AND FOLLOW-UP STUDY IN 29 CASES

By SIGURD EEK

From the Departments of Pediatrics and Pediatric Roentgenology of the University Clinic (Rikshospitalet)
OSLO, NORWAY

THERE are two main types of congenital duodenal obstruction: (1) *Intrinsic obstruction* due to anomalies *in* the wall of the duodenum itself, provoking stenosis; (2) *extrinsic obstruction* due to anomalies *outside* the duodenum, interfering with passage through the intestines.

Intrinsic duodenal obstruction (Fig. 1) occurs when the canalization of the intestines is disturbed between the fourth and tenth weeks of fetal life. The stenosis of the wall of the duodenum is classified according to the pathological-anatomical picture it presents.

(1) *Diaphragmatic or veil obstruction* which may be (a) complete, (b) with a single central opening (iris stenosis), (c) with several small openings, or (d) with only an insignificant, circular constriction of the wall of the duodenum not giving rise to clinical manifestations.

(2) *Canal stenosis* whose length and width may vary.

(3) *Atresias*. The two closed ends of the intestine may be different lengths apart, being connected only by a band-like survival of the primary gut or without any direct connection whatever with each other.

The atresias of the intestine are usually to be found in the ileum, being more rare in the duodenum and often multiple. The stenoses of the intestine are usually to be found in the duodenum and are said never to be multiple (Ladd and Gross[24]). The obstruction is usually caudal to the papilla of Vater, but it may also occur at the same level as, or oral to, this papilla.

Extrinsic duodenal obstruction occurs as a result of a pathological rotation of the intestine during fetal life, malrotation. The position of the small and large intestines becomes abnormal, and, as a rule, they share the same omentum which is very narrow and is known as the mesenterium commune. The cecum may be found in the extreme left flank somewhere in the upper abdomen or, on rare occasions, in the normal position, but with a long mesentery with the result that it moves freely. The ascending colon runs very often parallel with the transverse colon, the cecum being near the midline, in close relation to the third section of the duodenum (Fig. 2*A*).

As a rule, fibrous peritoneal bands pass from the cecum over to the duodenum, and they can extend from the cecum to the

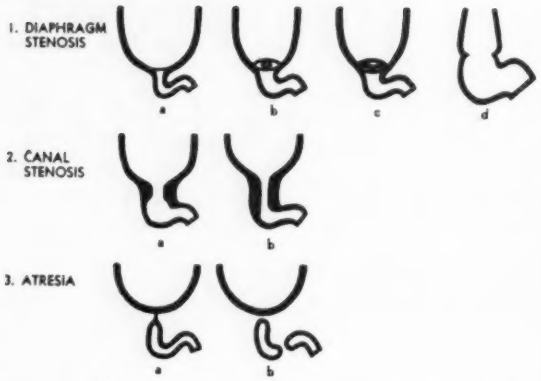


FIG. 1. Congenital Intrinsic Duodenal Obstruction.

1. Diaphragmatic or veil obstruction: (*a*) complete obstruction, (*b*) small central opening (iris stenosis), (*c*) multiple small openings in the diaphragm, (*d*) ring-shaped, insignificant constriction of the wall of the duodenum not constituting any obstruction and not giving rise to clinical manifestations.

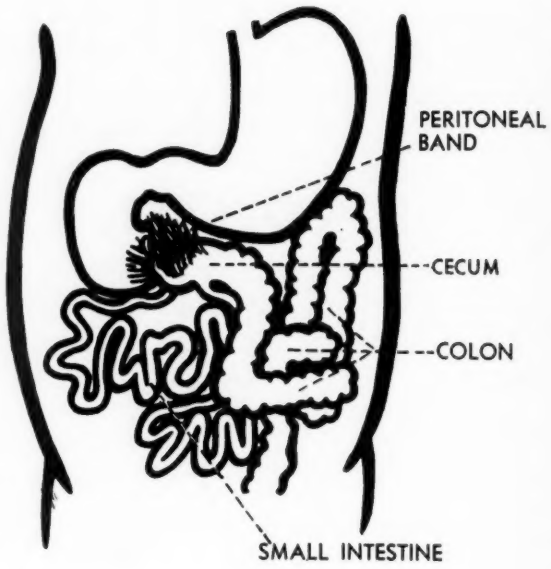
2. Canal stenosis: (*a*) short, but comparatively wide stenosis, (*b*) long and narrow stenosis.

3. Atresia: (*a*) The two closed sections of the intestine are connected with each other by a rudimentary band-shaped survival of the primary gut, (*b*) complete absence of any connection between the closed ends of the intestine. Both (*a*) and (*b*) can be multiple.

posterior abdominal wall or upward towards the gallbaldder or liver regions. These bands are now held to be congenital anomalies and not secondary adhesions. It is rare for malrotation of the intestine to exist without these peritoneal bands being present. They are one of the most common causes of congenital duodenal obstruction. The gastrocolic ligament is usually lacking, and the omentum hangs down freely from the greater curvature of the stomach.

The position of the duodenum may be normal, but it often runs an abnormal course in cases of malrotation. Its course may run more or less caudal, and it may be surrounded by peritoneal bands, with a more or less long mesentery. Or the duodenum may pass through the mesentery of the ileum, not infrequently right down to its opening into the cecum (Fig. 2*B*).

The gap in the mesentery may be so narrow that it gives rise to stenosis of the duodenum. The narrow root of the mesentery, which contains the superior mesenteric



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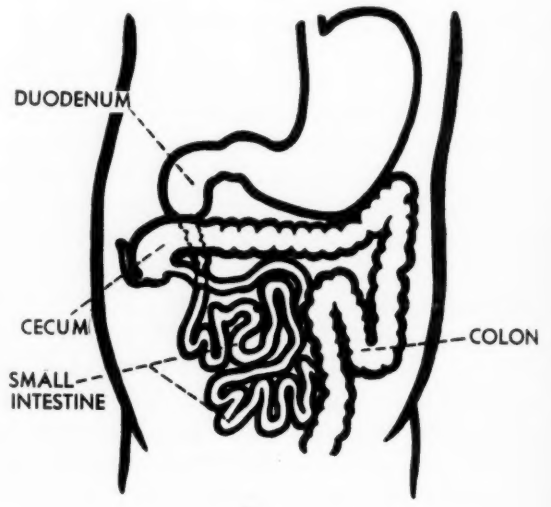

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FIG. 2. Congenital Extrinsic Duodenal Obstruction.

(*A*) Case 11. Malrotation of the intestine with constricting peritoneal bands. Postmortem findings: Practically the whole of the colon lay in its entirety in the *left* flank, the cecum being close to the duodenojejunal flexure. Constricting peritoneal bands passed from the cecum over to the duodenum, causing considerable obstruction. The small intestine lay in the *right* flank.

(*B*) Case 7. Malrotation of the intestine with pathological, peritoneal bands. Volvulus. The duodenum runs an abnormal course (for the sake of clarity the volvulus has been untwisted and the cecum turned over to the right in this diagram). Operative finding: Absence of the duodenojejunal flexure. The duodenum ran a straight

»»→

artery and vein, predisposes to volvulus whose onset provokes a greater or lesser degree of stenosis of the intestine, which usually corresponds to the duodenojejunal flexure. The circulation to and from that section of the mesentery and intestine which has undergone torsion is compromised, and as the compression of the artery is usually less than that of the veins, the result is a venous stasis with edema of the wall of the intestine and the corresponding mesentery. As a rule, the volvulus includes the whole of the fetal mid-gut, *i.e.*, all that section of the intestine which lies between the duodenum and the middle of the transverse colon. In a few cases the volvulus may be confined to only part of the mid-gut, for example the cecum only. In rare cases the volvulus occurs before birth, but, as a rule, it does so directly after birth, though it may set in at any moment in the patient's life. The degree of torsion varies greatly, from only a few degrees to more than one thousand (McIntosh and Donovan[27]). A combination of intrinsic and extrinsic obstruction can occur, but is rare (McIntosh and Donovan,[27] Hicken *et al.*[19]).

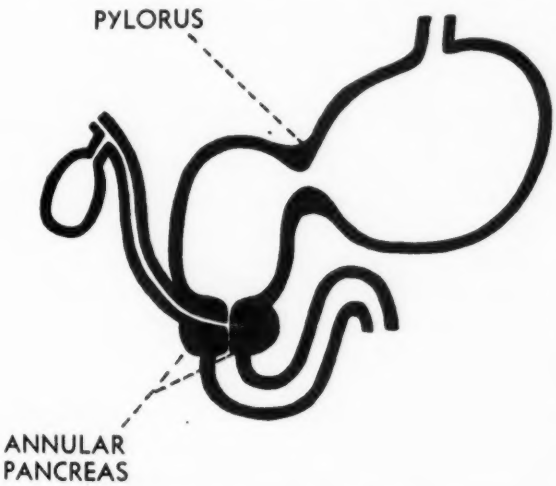


Fig. 3. Congenital Extrinsic Duodenal Obstruction. Case 23. Annular pancreas. Postmortem findings: The head of the pancreas forms a ring embracing the duodenum completely at the level of Vater's papilla. The stenosis opening was as small as a needle's point.

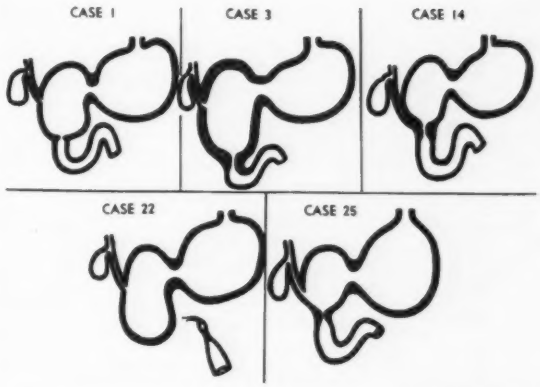


Fig. 4. Diagrams of the 5 patients with congenital intrinsic duodenal obstruction. Case 1: Diaphragmatic stenosis. Case 3: Canal stenosis with great thickening and hypertrophy of the wall of the duodenum. Case 14: Canal stenosis at the level of Vater's papilla. Case 22: Atresia without any connection between the two closed ends of the intestine. A closed cavity of the size of a pea was found in the cephalic end of the lower section of the intestine. Case 25: Short canal stenosis.

A rare case of congenital extrinsic duodenal obstruction is an annular pancreas whose head embraces the intestine, forming a constricting ring at the level of the papilla of Vater (Fig 3).

MATERIAL

The present material is based on 29 patients who in the course of the last twenty-five years (1927–1952) suffered from congenital obstruction of the duodenum, and who were treated in the Pediatric Department of the Rikshospital. There were 21 boys and 8 girls, and their ages ranged from two days to eleven years (Table 1).

The sex distribution of these cases differs from that of Webb and Wangensteen,[39] McIntosh and Donovan[27] and Ehrenpreis and Sandblom,[10] who found the sexes approximately equally represented. The relative number of intrinsic and extrinsic cases of obstruction did not differ materially from the findings of other observers (Ladd and Gross).[24]

The 29 patients are representative of the most common types of congenital, organic constriction of the duodenum, and some

caudal course, passing through a gap in the mesentary of the ileum, 2 cm. from Bauhin's valve. Passage through the duodenum was not greatly obstructed.

TABLE I

MATERIAL CLASSIFIED ACCORDING TO THE DIFFERENT TYPES

Group	Type of Obstruction	Case No.	Number of Cases	
I	Intrinsic duodenal obstruction			
	1. Diaphragmatic stenosis			
	(a) Incomplete	1	1	
	2. Canal stenosis	3, 14, 25	3	
	3. Atresia	22	1	5
II	Extrinsic duodenal obstruction			
	A. Malrotation with:			
	1. Peritoneal bands causing great stenosis	4, 5, 8, 9, 11, 15, 18, 20	8	
	2. Volvulus *with* no symptom-provoking peritoneal bands	2, 6, 7, 12, 13, 16, 17, 19, 21, 24, 26, 28, 29	13	
	3. Volvulus *without* peritoneal bands	10, 27	2	23
	B. Other causes			
	1. Annular pancreas	23	1	1
			Total	29

of the more rare types are lacking in this material.

There were not many cases of congenital malformations and genetically determined diseases in the families of these patients, the frequency of such ailments being hardly greater than in the community as a whole (Table II).

Two of the patients belonged to the same family, Case 1 being the father of Case 25. The mothers of the patients had undergone a total of 106 pregnancies, and their mean age when the patients were born was 30.7 years, an age practically the same as that of Norwegian mothers taken as a whole, 30.5 years in 1930 and 30.4 years in 1946 and 1947.

Table III gives the complications or abnormalities which befell the patients' mothers when they were pregnant with them. There was no case of measles, "influenza" or other infectious disease among these mothers. The number of abortions, 13 in all, which the 29 mothers underwent, did not differ much from the mean for Norweigan mothers as a whole in this respect. The place number of the patients in the sequence of births in each family did

TABLE II

DISEASES AND MALFORMATIONS IN THE FAMILY

Diseases and Malformations	Case No.	Intrinsic Duodenal Obstruction. No. of Cases	Extrinsic Duodenal Obstruction. No. of Cases
Diabetes	11, 12, 25	1	2
Congenital heart disease	1	0	1
Congenital hip luxation	17	0	1
Congenital duodenal obstruction	25	1	0
Total	6	2	4

TABLE III

PREGNANCIES

	Mothers of Case No.	Intrinsic Duodenal Obstruction. No. of Cases	Extrinsic Duodenal Obstruction. No. of Cases
Diseases (anemias)	6, 12	0	2
Abortions	5(3),* 8(2), 13(1), 20(4), 24(3)	0	5(13)
Uterine hemorrhage during first two months of pregnancy	20, 21	0	2
Polyhydramnion	23	0	1
Premature patients	18, 22, 23	1	2
Premature children in earlier pregnancies	13, 24	0	2
Total number of mothers with abnormal pregnancies	11	1	10

* The figures in parentheses give the number of abortions:

also not differ from the normal. Thus there was no support given by the present material to Landtman's[25] finding that malformations are more likely to occur among children born to elderly mothers, to children of mothers with a tendency to abort, or to children comparatively far out in the sequence of births in a given family.

Potter[33] states that polyhydramnion is common among mothers pregnant with infants suffering from permanent, organic constriction of the duodenum. Cordes[6] and Webb and Wangensteen[39] have shown that the incidence of premature births in their materials was greater than normal. In my material one mother suffered from polyhydramnion, and there were 3 patients premature at birth. These figures are in opposition to the conclusion that the above-mentioned observations reflect a general rule, but my patients are too few to justify the drawing of definite conclusions.

It may, however, be well to note that, according to Table III, the mothers with complications or abnormalities capable of interpretation as endometrial disturbances during their pregnancies gave birth to children with extrinsic obstructions, *i.e.*, conditions likely to arise during the organogenetic period of fetal life. The mothers who gave birth to infants with intrinsic obstructions suffered from no complica-

TABLE IV

INCIDENCE OF NONINTESTINAL MALFORMATIONS

	Case No.	Intrinsic Duodenal Obstruction. No. of Cases	Extrinsic Duodenal Obstruction. No. of Cases
Mongolian idiocy	3, 14, 16, 23	2	2
Meckel's diverticulum	22	1	0
Malformation of the left urinary tract	5	0	1
Malformed liver	13	0	1
Bilateral inguinal hernia	28	0	1
Umbilical hernia	5, 21	0	2
Total	9	3	6

TABLE V

ONSET OF THE SYMPTOMS AND TIME OF ADMISSION TO HOSPITAL

Age	Intrinsic Obstruction		Extrinsic Obstruction								Total			
			Malrotation with:						Annular pancreas					
			Obstructing bands		Peritoneal bands and volvulus		Volvulus							
	Onset	Admis.	Onset	Admis.	Onset	Admis.	Onset	Admis.	Onset	Admis.	Onset		Admis.	
1 wk.	5	2	7	2	6	1	2	2	1	1	21		8	
2 wk.		1	1	4	2	1					3	27	6	16
3 wk.		1			2	1					2		2	
4 wk.					1						1			
2 mo.				2									2	
3 mo.		1				1							2	
4 mo.						1							1	
5 mo.						1							1	9
6 mo.					1	1					1		1	
7 mo.						1							1	
9 mo.						1							1	
1 yr.					1						1			
2 yr.						1							1	
3 yr.						1							1	4
4 yr.						1							1	
11 yr.						1							1	
	5		8		13		2		1		29			

tions during their pregnancies. This form of malformation *can* be linked to the genes (see Cases 1 and 25 who belonged to the same family, and who both suffered from intrinsic duodenal obstruction). Other, nonintestinal malformations were found in 9 patients (Table IV).

Manifestations of Congenital Duodenal Obstruction. The chief manifestation was vomiting which often came in spurts and invariably consisted of the discharge of bile-stained fluid. This showed that the duodenal obstruction was at the level of, or caudal to the papilla of Vater. When the patients were infants, peristaltic movements were usually visible in the epigastrium, which is occasionally distended. Distention of the whole abdomen is rare. Dehydration with its usual sequels developed quickly. In one case the vomited fluid was blood stained. In no case were there signs indicative of aspiration of the contents of the stomach into the respiratory tract. The character of the food had no influence on the violence of the patients' reactions, and while half of them were breast fed, the other half were bottle fed.

In 16 cases there were records concerning meconium. In 4 of these cases there was complete duodenal obstruction, and in all of them the quantity, the consistency and macroscopic appearance of the meconium were normal.

My material presented, from the clinical point of view, two numerically equal, well defined groups. In the one, consisting of 14 patients, *uninterrupted* vomiting was the expression of a permanent duodenal obstruction which in some cases was due to intrinsic stenosis and in others to extrinsic stenosis. In the other group, consisting of 15 patients, the vomiting was *periodic*, and

TABLE VI

THIRTEEN PATIENTS SUFFERING FROM MALROTATION OF THE INTESTINE WITH PERITONEAL BANDS AND VOLVULUS

Case No.	Sex	Age at First Attack of Vomiting	Age on Admission	Duration of Attacks	Number of Attacks	Duration of Symptom-Free Intervals
2	♂	1 day	10 days	2–6 days	Two	3 days
6	♂	3 wk.	4 yr.	5–6 days	Numerous	3– 8 wk.
7	♀	3 days	3 wk.	1–2 days	Numerous	2–14 days
12	♀	14 days	4 yr.	2–7 days	Numerous	7 days to many months
13	♀	12 days	4 mo.	2–3 days	Numerous	6– 7 days
16	♂	1 day	5 mo.	2–7 days	Numerous	2– 4 days
17	♂	3 wk.	10 mo.	1 day	Numerous	1– 3 wk.
19	♂	7 days	11 yr.	1–8 days	Nuemrous	1 day to many months
21	♀	1 mo.	5 mo.	1–8 days	Numerous	6– 7 days
24	♂	3 days	3 yr.	2–3 days	Numerous	Weeks to months
26	♂	17 mo.	20 mo.	4 days	Two	Months
28	♂	6 mo.	6 mo.	5 days	One	Months
29	♂	1 day	6 days	2–3 days	Three	2 days to 3 weeks
	9 ♂ 4 ♀	Between 1 day and 17 mo.	Between 6 days and 11 yr.	1–8 days	Between one single and numerous	One day to many months

the stenosis was intermittent and always of the extrinsic type.

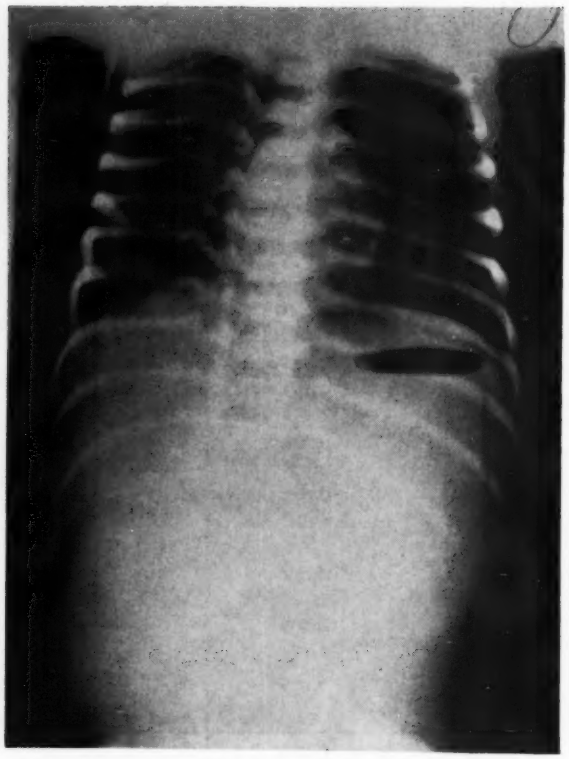
The patients suffering from uninterrupted vomiting belonged to the following types of duodenal obstruction (see Table 1): (a) intrinsic duodenal obstruction, (b) maltrotation with peritoneal bands causing great stenosis, (c) annular pancreas. The vomiting set in very soon after birth, during the first week of life with only one exception (Table v). The severity of the vomiting varied with the degree of stenosis, but was usually violent, and dehydration set in rapidly and led to early admission to hospital.

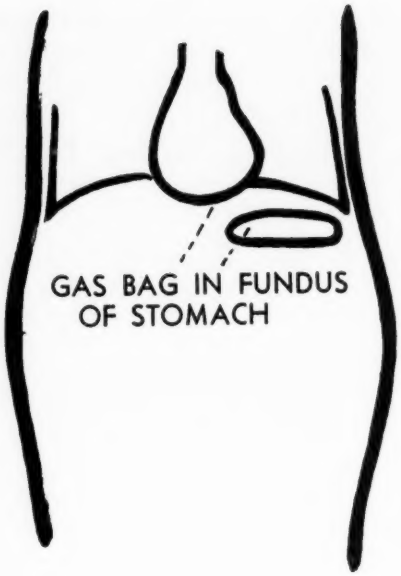
The patients suffering from periodic vomiting belonged without exception to the group characterized by malrotation of the intestine with volvulus. The vomiting was just as violent as in the preceding group, but it varied greatly in duration, from one to eight days (Table vi). These attacks of vomiting began without any demonstrable cause and ceased suddenly when for some unknown reason the volvulus was automatically corrected by untwisting. In several cases there was a short prodromal stage with anorexia, vomiting and abdominal pain. While the attacks of volvulus lasted, the bowel movements were often

TABLE VII

DATE OF ONSET OF SYMPTOMS

Patients with:	1st Day of Life	3rd Day of Life	1st Week	2nd Week	4th Week
Continuous vomiting	57%	78%	93%	100%	
Periodic vomiting	27%		53%		87%





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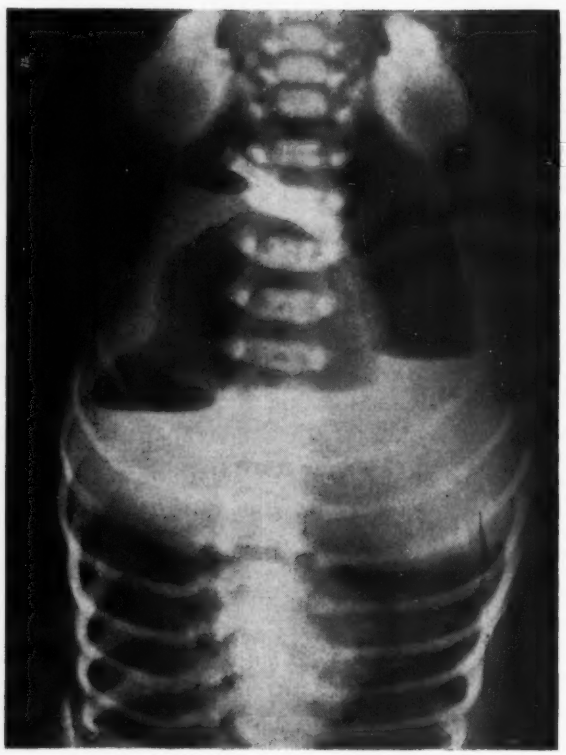
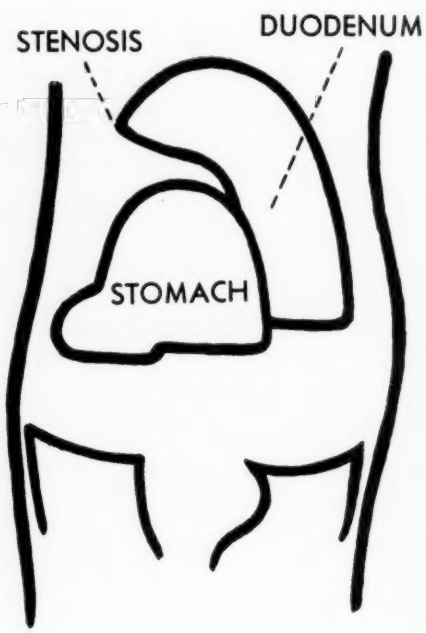




B

FIG. 5

scanty and liquid, hunger movements. When these attacks lasted a long time and followed each other in quick succession, the general condition deteriorated, weight became stationary or was lost, and the patients remained small and slender, becoming dystrophic.

The length of the free intervals between the attacks of vomiting also varied greatly, from one day to many months (see Table VI). In this group, too, the first attacks of vomiting began soon after birth, but they did so definitely later than the patients with permanent duodenal obstruction, and in one case the first attack began at the age of sixteen months (Table VII).

Discussion.

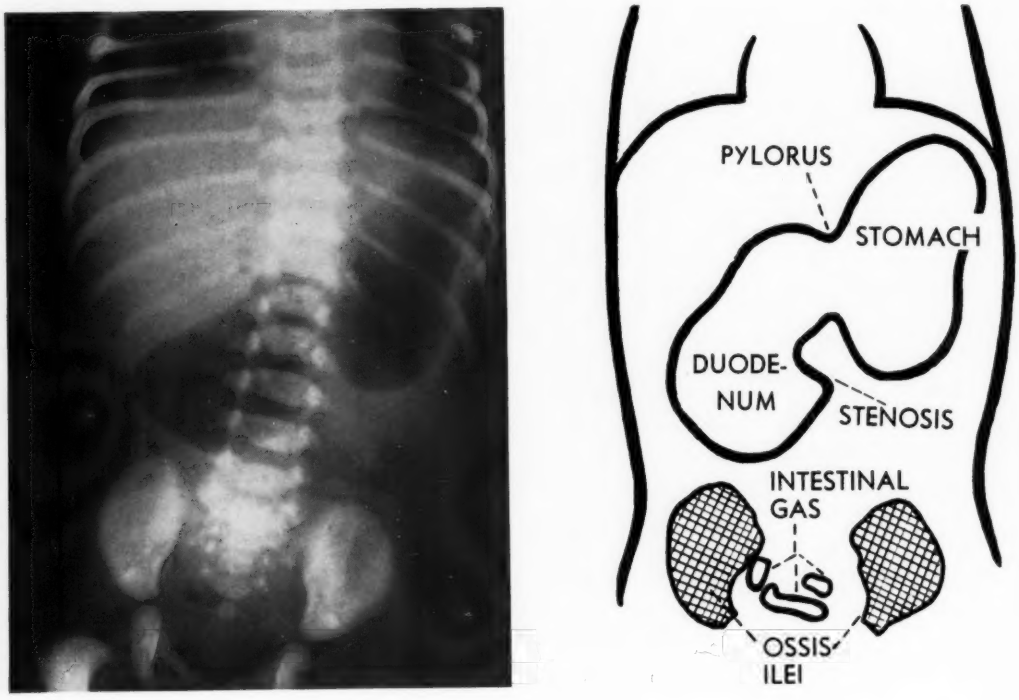
The general clinical picture presented by my patients does not differ in essentials from that of earlier publications (McIntosh and Donovan,[27] Ladd and Gross,[24] and Ehrenpreis and Sandblom[10]).

In cases with complete obstruction caudal to the papilla of Vater, the macroscopic appearance of the meconium was normal, an observation confirming that of Bolling[2] and Ladd and Gross[24] who found that the appearance of the meconium does not justify the drawing of any conclusion with regard to the presence or absence of an atresia of the intestinal tract. Only the microscopic examination carried out in the manner adopted by Farber[12] can make this point clear. None of the 8 patients with malrotation of the intestine and peritoneal bands causing great steonsis had ever suffered from volvulus. However a patient belonging to this type (Case 6) developed postoperative volvulus and died. On the other hand, none of the volvulus patients suffering from malrotation and undergoing operation presented peritoneal bands interfering with passage through the intestine (see Table I). It would therefore seem that peritoneal bands causing severe stenosis prevent volvulus in patients with malrotation. The best explanation of this conclusion is that the intestine caudal to the stenosis (the mid-gut) never runs the risk of being exposed to overloading by large quantities of chyle or to great digestive activity. Thanks to the obstruction of the intestine, its contents will always present a modest volume, digestive activities will be slight, and the weight of the mid-gut insignificant. Patients subject to recurrent volvulus should always take small and frequent meals containing little fluid. This rule also applies to patients who have been operated on because of severe stenosis produced by peritoneal bands and malrotation.

The possibility that the weight of the mid-gut may play a certain part in provoking volvulus in the subjects of malrotation has been indicated by Olsen[30] who has noticed that the subjects of malrotation often develop volvulus after intra-abdominal operations even when they have hitherto never presented manifestations of this deformity. His explanation of this phenomenon is that after such an operation, particularly when postoperative paralysis sets in or the intestines are overloaded with fluid, they promote the development of volvulus solely by virtue of their weight. Or interference with the circulation of the blood can be the heavy drag on the narrow mesentery.

On the clinical evidence, it is impossible to achieve a *differential diagnosis* between the various types of duodenal obstruction leading to continual vomiting. Recurrent attacks of bile-stained vomiting are most likely to indicate malrotation of the intestine with volvulus.

Fig. 5. Congenital Intrinsic Duodenal Obstruction. Case 22: (*A*) The patient was examined roentgenologically in the vertical position, head up. Apart from a small sac of gas in the fundus of the stomach with a basal fluid level, the whole of the abdomen is seen to be homogeneously dense, without gas in the intestines. (*B*) After 200 ml. of fluid had been aspirated from the stomach, the patient was examined in the vertical position, head down. The stomach and duodenum are enormously dilated, and the latter ends by tapering off conically in the entrance to the pelvis, to the left of the midline.


PYLORUS
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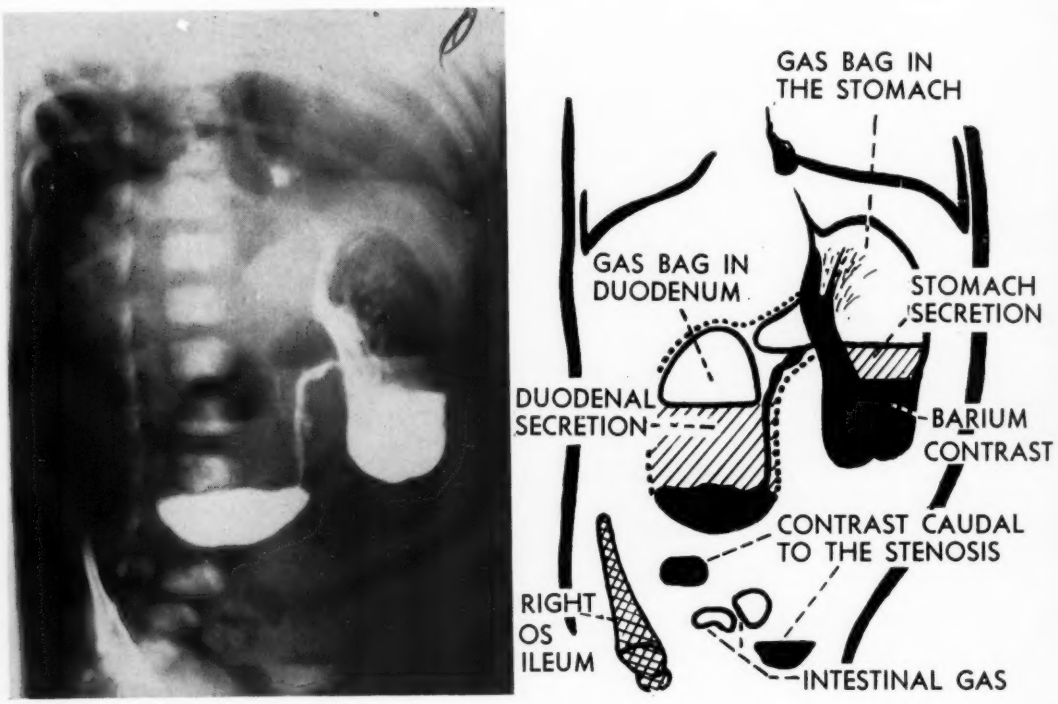
ILEI

A


GAS BAG IN
THE STOMACH
GAS BAG IN
DUODENUM
STOMACH
SECRETION
DUODENAL
SECRETION
BARIUM
CONTRAST
CONTRAST CAUDAL
TO THE STENOSIS
RIGHT
OS
ILEUM
INTESTINAL GAS

B

Fig. 6

Conclusion.

1. The violence of the manifestations of congenital, organic duodenal obstruction is proportional to the degree of the stenosis present.

2. If the cause of the obstruction acts permanently, the clinical manifestations is the same whether the stenosis is extrinsic or intrinsic.

3. The volvulus in cases of malrotation of the intestine is, as a rule, intermittent. The first attack may come at any age, but is most common in the neonatal period.

4. Individuals with malrotation of the intestine should never overload the intestines with large quantities of food and/or fluids.

THE ROENTGENOLOGICAL EXAMINATION

Among the 29 patients in my material were 25 who underwent roentgen examination, in 24 cases with a barium contrast meal.

Roentgenological Technique. The patient's stomach and duodenum are evacuated as effectively as possible by aspiration before the roentgen examination which starts with the taking of a plain roentgenogram of the abdomen, the patient being in the horizontal position and the direction of the rays being vertical. If need be, a preliminary inflation of the stomach and duodenum with air is undertaken according to the technique of Mellins and Milman.[28] The next step is an examination with the rays horizontal and the patient lying on the right and left side respectively and vertically, with head up and head down. When the clinical evidence raises a suspicion of recurrent volvulus, the next step should be a barium examination of the colon, and only when this is completed should the stomach and duodenum be examined in the same way, for the volvulus may be successfully corrected by a barium enema (see Fig. 9). For the examination of the stomach and duodenum, the barium is introduced directly into the former through a stomach catheter. About 10 ml. of a comparatively dilute contrast solution is sufficient for a newborn infant. When the examination is completed, as much as possible of the barium contrast is aspirated.

A roentgenological examination is the only preoperative device by which the suspicion of obstruction in the duodenum can be confirmed or disproved. When it is the former, the evidence on which confirmation is based usually consists of enormous dilatation of stomach and duodenum oral to the obstruction, the degree of dilatation being, as a rule, proportional to the degree of the stenosis. The dilated duodenum is not infrequently atonic and larger than the stomach, and the opening of the pylorus is often wide. When the stenosis is complete and has existed from before birth, no intestinal gas is to be seen caudal to the obstruction (Fig. 5, *A* and *B*). However, this may also be the case if a complete stenosis due to the volvulus has existed for some days.

If passage through the stenosis is difficult, only quite small bubbles of gas will be seen and perhaps small patches of the contrast medium caudal to the obstruction. In such cases there will also be considerable dilatation of the stomach and duodenum (Fig. 6, *A* and *B*).

It will be difficult from examination of the stomach and duodenum alone to decide whether the obstruction is intrinsic or ex-

Fig. 6. Congenital Extrinsic Duodenal Obstruction. Case 27: Malrotation of the intestine with pathological peritoneal bands and volvulus. (*A*) Examination in the supine position. Stomach and duodenum enormously dilated. Pylorus wide open. The conically formed duodenal obstruction projected on the vertebral column. Small bubbles of gas in coils of intestine in the true pelvis. (*B*) Examination in the vertical position, head up. A barium contrast, 10 ml., introduced into the stomach through a catheter. The stenosed duodenum hangs like a large and slack sac with the barium contrast at the bottom. Above the contrast material there is a thick layer of fluid, and over it again is a large sac of gas. The stomach is somewhat smaller than the duodenum, but with the same stratification of its contents, air, fluid and barium contrast. The pylorus is wide open, and on tipping the patient sideways, the contrast runs unhindered down to the bottom of the duodenal sac. Small quantities of gas and contrast distal to the small intestine.

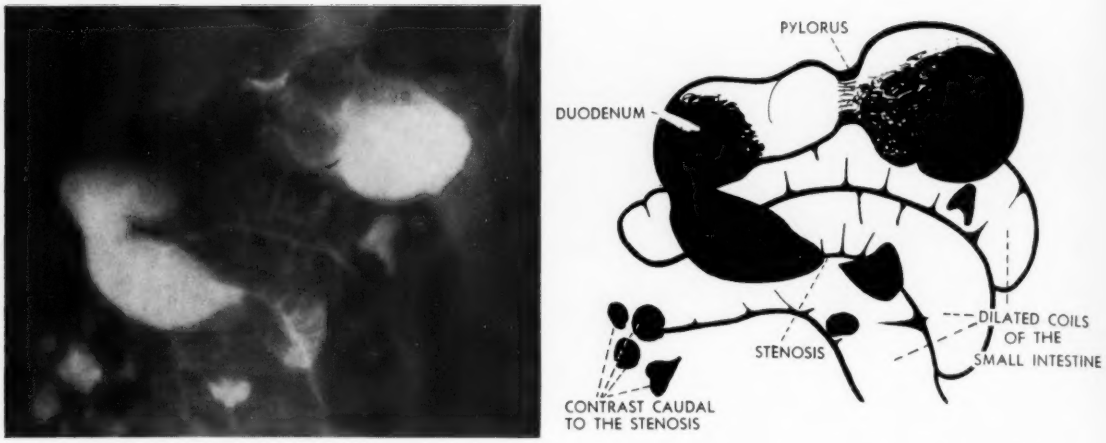


FIG. 7. Congenital Extrinsic Duodenal Obstruction. Case 16: Malrotation of the intestine with pathological peritoneal bands and volvulus of the mid-gut which *has lasted several days*. The stomach is seen to be somewhat dilated but is much smaller than the duodenum whose distal section, filled with contrast material, tapers off conically towards the stenosis. The pylorus is wide open. Caudal to the stenosis are several much dilated, gas-filled coils of small intestine running parallel to each other. There are small quantities of contrast medium in the dilated coils of the small intestine.

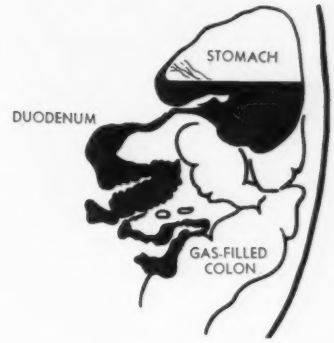
trinsic. Apart from the very rare cases in which an intrinsic and an extrinsic stenosis exist simultaneously, or in which there is an annular pancreas, this point will be decided by a barium enema of the colon. The stenosis must be extrinsic when there is a malrotation of the intestine, and extrinsic when the position of the colon is normal.

Directly after volvulus has occurred, the intestine caudal to the site of the volvulus in the duodenum will contain little gas and will have collapsed. If the stenosis is incomplete, small quantities of swallowed air, coming from the stomach and duodenum, will make their way from time to time through the intestine. But if the passage through the *cranial* intestinal stenosis is comparatively free, while the *caudal* stenosis, usually situated in the middle of the transverse colon, is involved in a complete stenosis, a considerable and growing dilatation of the twisted section of the intestine will be found after the volvulus has lasted for some days (Frimann-Dahl[14]). This is what happened in Case 16 (Fig. 7). This distention of the whole of the abdomen hides the stenosis of the duodenum whose demonstration can be effected only by means of a barium meal given by mouth. When the volvulus is corrected spontaneously or by operation, the stomach and duodenum quickly regain their normal size and shape (Fig. 8, *A*, *B*, *C*, *D* and *E*). On the other hand, dilatation sets in very quickly after development of volvulus (Fig. 8, *C*).

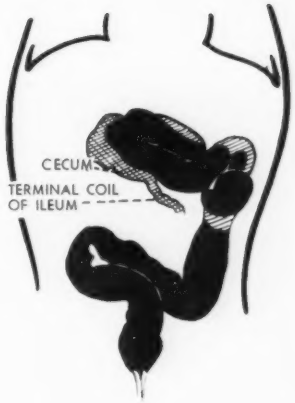
In one case a volvulus was successfully untwisted with the help of a diagnostic barium enema (Fig. 9, *A* and *B*).

Discussion.

Several authors (Bayer,[1] Cohen,[5] Ladd and Gross[24] and Mellins and Milman[28]) are opposed to the routine employment of barium meal by mouth for the roentgenological examination of these patients because of the risk of aspiration into the respiratory passages of the contents of the stomach mixed with the barium contrast. Dannenberg *et al.*[7] add another contraindication: The barium contrast can cork up a stenosed opening through which passage has already been impaired. All my roentgenologically examined patients were given barium contrast by mouth with only one exception, and in no case were there any complications. In my experience the use of small quantities of barium contrast



A



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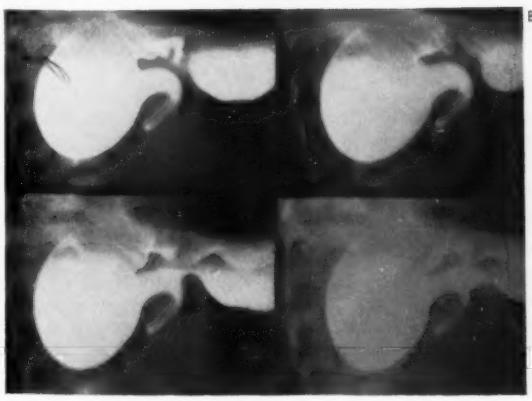
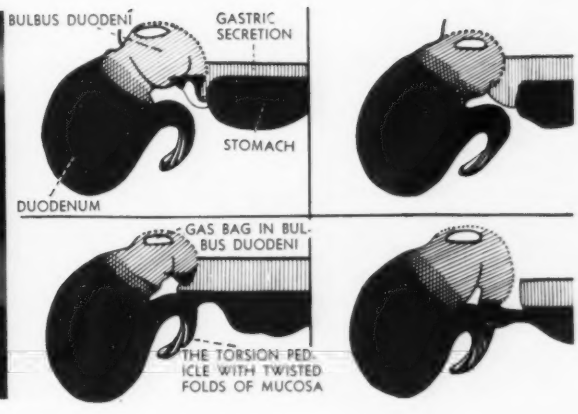
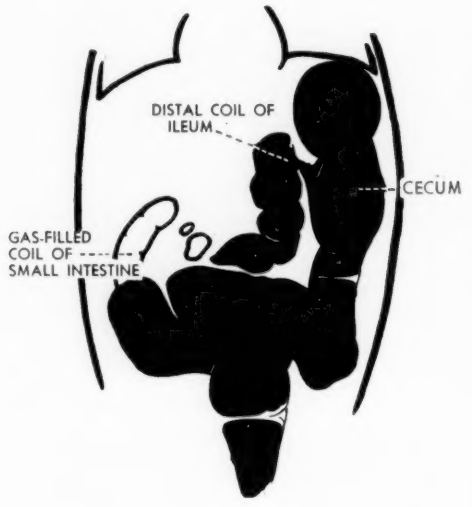


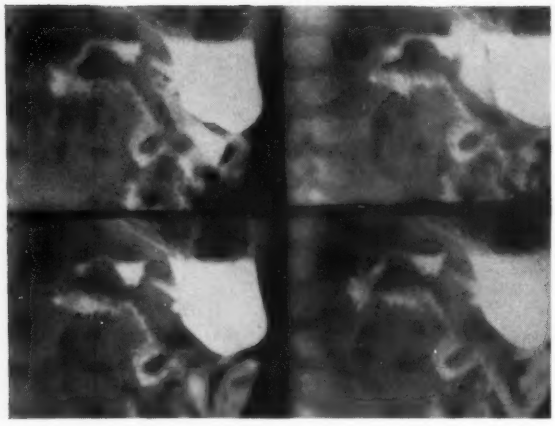


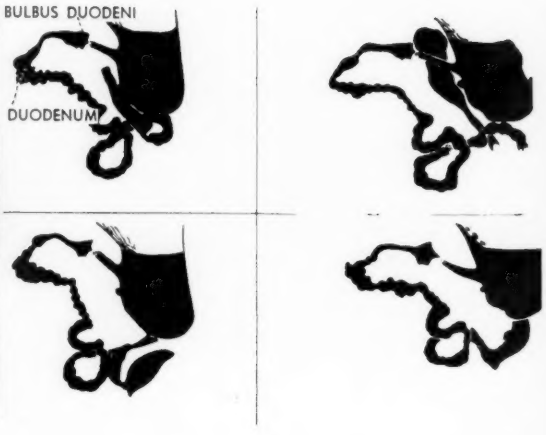
C

Fig. 8. (*Legend on p. 726*)



D





E

Fig. 8. Case 29. A seven day old boy came of a healthy family. His mother was twenty years old and a primipara without a history of earlier abortions. No illnesses during her pregnancy, which ran a normal course. Confinement at term and without complications. The appearance of the meconium, passed since the first day of life, was normal. When only a few hours old, the infant had frequent attacks of bile-stained, projectile vomiting, which suddenly ceased after they had lasted two days. After two more days of complete freedom from symptoms he began again to suffer from the same projectile vomiting, which continued till his admission to hospital three days later. On reaching the hospital he ceased to vomit, and apart from a slight degree of dehydration, the clinical examination was negative.

The roentgenological examination (*A*) showed normal conditions apart from a doubtful dilatation of the duodenum. Passage of contrast medium through the duodenum was unhindered. Examination of the colon (*B*) showed a malrotation of the colon with the ascending colon running parallel to the transverse colon and cecum situated in the middle of the epigastrium.

During the following three weeks the patient was quite free from symptoms, the dehydration passed off quickly, and there was a gain of weight. Then suddenly one night, for no demonstrable reason, he again

⇝

entails no risk when the patient's stomach and duodenum are aspirated before and after the examination and are kept empty until the obstruction is overcome. In some cases (see Case 16, Fig. 7) it is impossible to demonstrate stenosis of the duodenum without employing the contrast test.

The untwisting of a volvulus by means of a barium enema in cases of malrotation of the intestine has apparently not hitherto been put on record. The success of this measure depends on the fact that a mid-gut volvulus includes some of the colon, the section from the cecum to the middle of the transverse colon. The facility with which a malrotation volvulus often corrects itself spontaneously suggests that a barium enema can also initiate the process of correction. In our experience with the roentgenological untwisting of volvulus of the sigmoid, it is, however, probable that the untwisting of a volvulus of more than 360° will be difficult.

Conclusion.

1. Provided certain precautions are taken, the employment of barium sulfate by mouth does not entail any risk in the roentgenological examination of these patients.

2. When the patient's condition permits of an examination of the colon, this measure should not be omitted for two reasons—diagnostic and therapeutic. With regard to diagnosis, we wish to learn whether malrotation of the intestine does or does not exist. If it does, the stenosis of the duodenum will, in practically every case, be extrinsic. With regard to treatment, the object of this measure is to seek to untwist a volvulus of the mid-gut.

OPERATIVE TREATMENT

Among the 29 patients were 23 operated on. There were 3 postoperative deaths. Case 11 died of postoperative volvulus, Case 15 of postoperative paralytic ileus, and Case 22 of a faultily made anastomosis. Four patients were for various reasons operated on again (Table VIII). Seven different surgeons performed these operations, and the number of different methods was still greater (Table IX).

The highest degree of twisting in cases of malrotation volvulus was stated to be 360° clockwise and it usually measured 180°. The first operation was carried out in 1928 and was successful.

Up to 1945, the claims made for preoperative and postoperative treatment were comparatively modest. Before this date the postoperative reaction was usually violent, the case running a stormy postoperative course. Since 1945 the treatment given both before and after operation has been most carefully regulated, and the 13 patients operated on since this date have shown a very slight postoperative reaction. Of late years the Abbott-Rawson tube has been used on every patient undergoing enterostomy.

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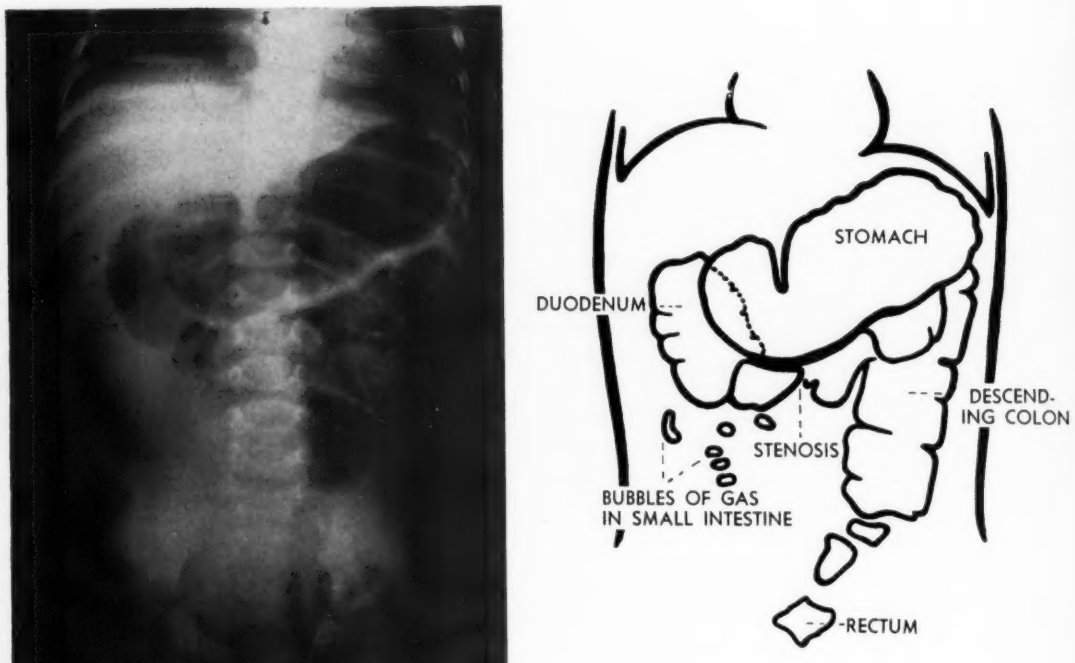
suffered from severe bile-stained vomiting in spurts. A roentgen examination six hours later (*C*) showed considerable dilatation of the duodenum with profuse secretion, although 120 ml. of fluid had previously been aspirated. The stalk of the volvulus appeared as a bird's beak with sharply defined folds of twisted mucous membrane. There were insignificant quantities of gas caudal to the stenosis. An hour later small patches of the contrast material could also be seen in the jejunum.

After as much as possible of the retained fluid and of the contrast medium had been aspirated, Ladd's operation was performed. The midgut was twisted 180° about a quite narrow root of the mesentery. Numerous peritoneal bands were detached and the colon was placed in the *left* flank, without fixation (*D*) and the small intestine was placed in the *right* flank. The patient was in excellent condition after the operation, and a roentgen examination of the stomach and duodenum (*E*) showed that the size of the stomach was normal, and the passage through the duodenum was unhindered. The duodenum was situated more vertically than it had been before the operation, and cranial to the jejunum a horseshoe-shaped coil, whose appearance did not change, was interpreted as indicating peritoneal bands which had not been detached during the operation.


STOMACH
DUODENUM
DESCEND-
ING COLON
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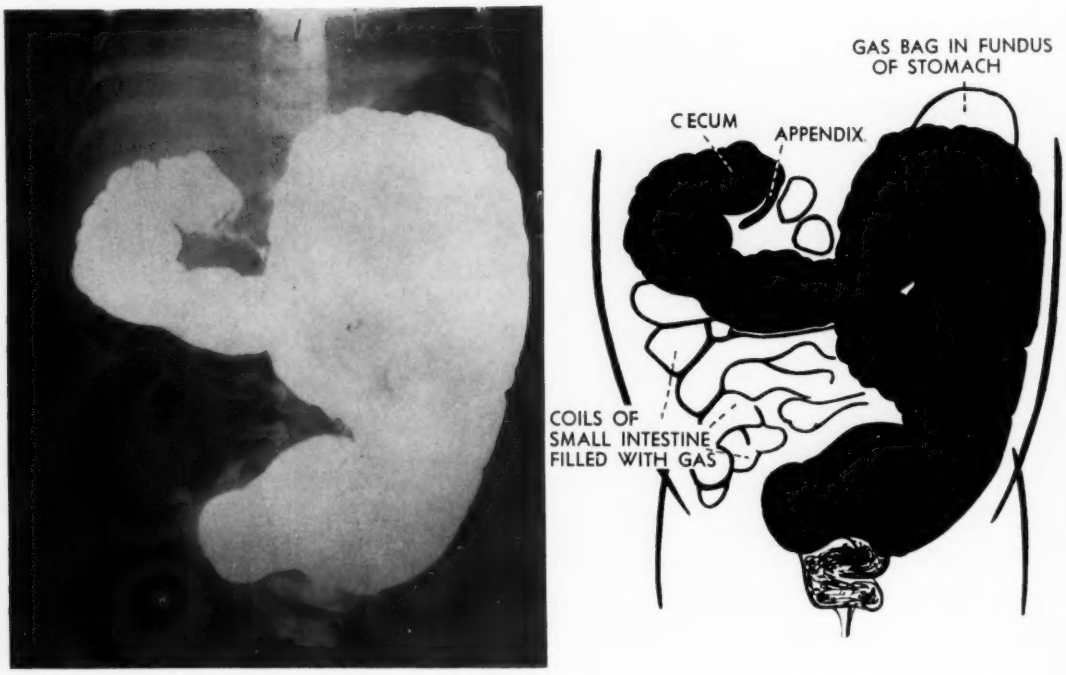
BUBBLES OF GAS
IN SMALL INTESTINE
RECTUM

A


GAS BAG IN FUNDUS
OF STOMACH
CECUM
APPENDIX
COILS OF
SMALL INTESTINE
FILLED WITH GAS

B

Fig. 9

TABLE VIII

RE-OPERATED PATIENTS

Case No.	First Operation	Postoperative Complications	Days Passed Since First Operation	Re-operation	Result
6	Detorsion and lysis	Poor passage through duodenum	10	Gastrojejunostomy	For some years abdominal pain and borborygmi; well last 4 years
12	Detorsion and gastrojejunostomy	Volvulus with uncertain passage through duodenum	16	Detorsion and duodenojejunostomy	Well except for diarrhea after fatty meals
15	Lysis	Ileus (atony of the duodenum)	4	Duodenojejunostomy	Died
24	Lysis	Hernia of abdominal wall with incarceration	10	Lysis	Volvulus 3 months after last operation; subsequently symptom free

Discussion.

As Table x shows, the primary operative result was very satisfactory in comparison with the material of other authors. It is difficult to find any explanation for the very low postoperative mortality in the present material. There is nothing to show that its character or the preoperative state of the patients differed from that of other material. My own material does not differ from other material with regard to the interval between the onset of symptoms and admission to the hospital.

Conclusion.

1. The choice of mode of operation does not seem to have been of any importance in the primary operation result provided

FIG. 9. Case 21. A girl, six months old, weighed 3,750 grams at birth when she was 50 cm. long. She came of healthy stock, and her elder brother was healthy. At the time of her birth her mother was thirty-seven years old. Pregnancy had run a normal course, without any illness, and confinement at term had been normal. The mother had not suffered from earlier abortions. After being breast fed for three months, the patient was artificially fed. When six weeks old, she suddenly, and for no demonstrable reason, began to suffer from several daily attacks of bile-stained projectile vomiting. The attacks continued *periodically*. At first she was free from these attacks for two to four days at a time, and thereafter they would return suddenly. Now and then these free intervals lasted up to a fortnight. The infant's physical condition was unsatisfactory, and gain of weight was very slow. During the last two months before admission to the hospital the attacks of vomiting had again become more frequent, and the free intervals had constantly become shorter. Her weight steadily declined, and when she was admitted to the hospital, six months old, her condition was deplorable, and she showed marked dehydration and weighed 4,000 grams, or only 250 grams more than she had weighed at birth, whereas the normal weight for an infant of her age is 7,100 grams. A physical examination showed a sunken abdomen and marked general dehydration.

A roentgenological examination in the supine position (*A*) showed a much dilated stomach and duodenum with open pylorus. The duodenum ended in the caudal direction by tapering off conically. A few quite small bags of gas could be seen in the small intestine in the right flank. In the left flank there were coils of colon well filled with gas (evacuation enema). They corresponded to the descending colon and the sigmoid. Directly after this examination, a diagnostic barium enema was given. It showed (*B*) malrotation with the cecum situated under the liver. While the barium enema was being given, numerous coils of small intestine in the right flank suddenly became filled with considerable quantities of gas. *The volvulus existing on this occasion became untwisted by the help of the barium enema.*

After this examination the patient was entirely free from vomiting for two days, after which it set in again. Volvulus developed again, and the patient was transferred to a surgical department for operation.

Operation. The volvulus had become untwisted either immediately before the operation, or the operator had succeeded in doing so without his knowledge. Numerous peritoneal bands passing from cecum to duodenum and posterior abdominal wall were detached. None of them interfered with passage through the intestines.

TABLE IX

METHODS OF OPERATION

Number of Methods	Methods of Operation	Intrinsic Obstruction Case No.	Extrinsic Obstruction Case No.	Total
1	Lysis	—	4, 5, 9, 11, 15, 21, 24 (twice) 28	9
2	Detorsion	—	10	1
3	Detorsion and lysis	—	2, 6, 26, 29	4
4	Detorsion and gastrojejunostomy	—	12, 19, 27	3
5	Detorsion and duodenojejunostomy	—	12	1
6	Gastrojejunostomy	3	6, 8, 16, 18, 20	6
7	Duodenojejunostomy	25	15	2
8	Gastrocolostomy	22		1
		3 patients	20 patients 4 re-operated	27

the obstruction was overcome.

2. A careful and correct preoperative and postoperative treatment is of the greatest importance to the postoperative course of these cases.

THE FOLLOW-UP EXAMINATION

Nineteen of the 20 patients surviving the operation were successfully traced. The missing patient (Case 3) had been perfectly symptom-free since her operation for an intrinsic stenosis, but she died when a year old of an intercurrent disease. The observation period for the 19 survivors ranged from four months to twenty-three years (Table XI).

Fifteen of these 19 patients have been perfectly symptom-free since they were discharged from the hospital. Among the remaining 4 patients there were 3 with transitory troubles which disappeared long ago. Only 1 patient (Case 12) has still some trouble related to the digestive tract, but it is just as probable that her symptoms can be traced to her two anastomoses as to her primary malformation. The 4 patients with postoperative abdominal symptoms were as follows:

CASE 5. This patient was born in 1936, and was operated on when seventeen days old. There were two attacks of abdominal pain taken to indicate volvulus, the one attack four months after the operation, the other eleven years after it. On both occasions the attack passed off without an operation being necessary. In 1944, he was operated on for a malformation of the urinary tract on the left side. He has been perfectly symptom-free for the last five years.

CASE 6. This patient, born in 1933, was operated on when four years old. For some

TABLE X

Author	Year	Intrinsic Duodenal Obstruction		Extrinsic Duodenal Obstruction	
		Operation	Recovery	Operated	Recovery
McIntosh and Donovan[27]	1939			18	12
Ladd and Gross[24]	1941	16	8	44	27
Swenson and Ladd	1945	24	8		
Ehrenpreis[10]	1949	20	9		
Eek	1952	3	2	20	18

Table XI

TYPE OF OPERATION AND FOLLOW-UP EXAMINATION

Case No.	Age at Operation	Type of Operation	Time Passed Since Operation	Follow-up Examination
		Group I. Intrinsic Duodenal Obstruction		
3	7 mo.	Gastrojejunostomy	4 mo.	Symptom-free until, 4 mo. after discharge from hospital, the patient died of an intercurrent disease
22	6 days	Gastrocolostomy	—	A postoperative death
25	6 wk.	Duodenojejunostomy	8 mo.	Symptom-free
		Group II. Extrinsic Duodenal Obstruction		
		A_1 Malrotation with Obstructing Peritoneal Bands		
4	6 wk.	Lysis	17 yr.	Symptom-free
5	17 days	Lysis	16 yr.	Volvulus 4 mo. and 11 yr. after operation. Operated on when 8 yr. old for a malformation of the urinary tract, well during the last 4 yr.
8	9 wk.	Gastrojejunostomy	13 yr.	Symptom-free
9	15 days	Lysis	12 yr.	Symptom-free
11	6 days	Lysis	—	A postoperative death
15	6 days	1) Lysis 2) Duodenojejunostomy	—	A postoperative death
18	4 days	Gastrojejunostomy	4 yr.	Symptom-free
20	4 days	Gastrojejunostomy	4 yr.	Symptom-free
		A_2 Malrotation with Peritoneal Bands and Volvulus		
2	15 days	Detorsion and lysis	23 yr.	Symptom-free
6	4 yr.	1) Detorsion and lysis 2) Gastrojejunostomy	15 yr.	Attacks of abdominal pain for some years. Symptom-free the last 12 yr.
12	4 yr.	1) Detorsion plus gastrojejunostomy 2) Detorsion plus duodenojejunostomy	8 yr.	Symptom-free except for diarrhea after very fatty food
16	5 mo.	Gastrojejunostomy	$4\frac{1}{2}$ yr.	Symptom-free
19	11 yr.	Detorsion and gastrojejunostomy	4 yr.	Symptom-free
21	6 mo.	Lysis	$1\frac{1}{2}$ yr.	Symptom-free
24	2 yr.	1) Lysis 2) Lysis	$1\frac{1}{2}$ yr.	Volvulus 3 mo. after operation. Since then symptom-free
26	2 yr.	Detorsion and lysis	7 mo.	Symptom-free
28	3 yr.	Lysis	$2\frac{1}{2}$ yr.	Symptom-free
29	1 mo.	Detorsion and lysis	2 mo.	Symptom-free
		A_3 Malrotation and Volvulus		
10	12 days	Detorsion	9 yr.	Symptom-free
27	6 mo.	Detorsion and gastrojejunostomy	6 mo.	Symptom-free

years he was subject to colicky abdominal pain followed by borborygmi. He has been perfectly well during the last four years.

Case 12. This patient, born in 1940, was operated on when four years old; is subject to slight transitory diarrhoea with a moderate degree of pain, particularly after meals rich in fats. No other symptoms.

Case 24, born in 1946, was operated on when two years old. Three months after the operation an attack of volvulus set in and lasted two days before it disappeared. Patient has been perfectly well since then.

Three of these 4 patients (Cases 6, 12 and 24) were operated on twice during the same stay in a hospital for their malformation. The fourth patient (Case 5) suffered for several years after the operation for stenosis of the duodenum from an anomaly which concerned the urinary tract and which gave rise to symptoms until he was operated on for it eight years later.

One of the surviving patients was a mongoloid. All the other patients were mentally normal. The physical development was normal for all except Case 12 who experienced a moderate degree of discomfort over the digestion of fats. She was small and slender.

The roentgenological examination of the surviving patients showed that one of them, who had undergone gastrojejunostomy, had no free passage through the enterostomy opening. This opening functioned well in the other patients who had undergone gastrojejunostomy without any sign of peptic ulcer.

Discussion.

Here again it would seem that the choice of method of operation did not influence the late results. This is surprising, particularly in connection with a gastrojejunostomy which long ago was discredited because of its tendency to provoke jejunal ulceration. Bruusgaard[3] has shown that between 35 and 50 per cent of all adult patients undergoing gastrojejunostomy develop jejunal ulcers in the course of a few years after operation. Experience with my material suggests that children are much more likely to escape jejunal ulcers after gastrojejunostomy than adults. This comparison is, however, not quite fair as none of the children operated on had presented any sign of gastric ulcer in advance. Besides, for the comparison to be invalid the number of my patients is too small, and the observation period too short for the 8 patients surviving gastrojejunostomy (15, 13, 8, 4½, 4, 4, 4 and ½ years respectively). We have yet to learn whether these patients will or will not develop jejunal ulcers when they grow up.

Among the 4 patients with abdominal symptoms during the observation period there were 3 (Cases 6, 12 and 24) who were operated on again a few days after the first operation. The fourth patient (Case 5) was operated on when eleven years old for a malformation of the urinary tract on the left side. It would therefore seem that the patients who can pass through the postoperative phase without a second operation have an excellent chance to escape late sequels.

The reason why recurrence of volvulus is not more common after the operation may be that postoperative adhesions form between the intestine and abdominal wall comparatively early, the intestine becoming immobilized. It would seem that this happens whether the small and large intestine are dissected free and secured in place according to Ladd's technique, or the operation is limited to correction of the volvulus and an extemporaneous, local detachment of the peritoneal band in the duodenal area. Confirmation of the adhesion theory is to be found in the observation that when a volvulus recurs, it does so soon after the operation (see Cases 11 and 12).

Conclusion.

1. The follow-up examination of 19 survivors after operation for congenital, organic duodenal obstruction suggests that the risk of the development of jejunal ulcers in children in whom a gastrojejunostomy has been established is small. But as we have yet to learn whether this com-

parative immunity will persist after the patient has grown up, it seems best to avoid a gastrojejunostomy as often as possible.

2. Although it does not seem to be absolutely necessary in cases of malrotation of the intestine to undertake meticulous detachment of the fibrous peritoneal bands with placing of the small intestine in one abdominal flank and the large intestine in the other after the method of Ladd, this operation is yet the most logical and rational. If, however, the patient's general condition during the operation is such that there is no time for more than untwisting of a volvulus and/or a strictly local detachment of peritoneal bands about the duodenum so as to eliminate the stenosis, the patient still has a good chance to avoid late relapses.

3. The reason why postoperative late relapses are so rare seems to be that the intestine becomes fixed to the abdominal wall by adhesions.

4. When relapses occur, they do so most frequently directly after the operation, and it would seem that patients reoperated on are more likely to develop late sequels than others.

SUMMARY

The present material consists of 29 patients suffering from congenital, organic duodenal obstruction which was due to intrinsic stenosis in 5 and extrinsic stenosis in 24. In this latter group was one patient whose obstruction was due to an annular pancreas. The other 23 patients belonged to the group: malrotation of the intestine with or without volvulus.

Vomiting of bile-stained material with secondary desiccation dominated the clinical picture in every case. When the stenosis of the duodenum was permanent, whether it was of an intrinsic or an extrinsic character, the vomiting was continuous. All the patients with malrotation of the intestine and volvulus suffered from periodic attacks of vomiting.

A detailed account is given of the roentgenological examination, on which the diagnosis depends, and a case is recorded in which a volvulus was untwisted with the help of a barium enema.

Six patients died without any surgical intervention. Among the 23 cases operated on there were 3 postoperative deaths. The operations performed varied greatly in technique. Among the 20 patients who survived the operation was one whose late death was due to an intercurrent illness. The other 19 patients were alive from four months to twenty-three years after the operation. All have been re-examined, and 18 of them have been found to be perfectly well on re-examination. Three had experienced passing troubles since the operation, and the remaining 15 had had no discomfort since discharge. The one patient who was still subject to abdominal discomfort was but slightly troubled by it. Among 8 patients surviving gastrojejunostomy there was not one who developed ulcer of the jejunum.

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CEREBRAL ANGIOGRAPHY BY AN INTRAVASCULAR INTUBATION TECHNIQUE*

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CEREBRAL angiography is the roentgenographic visualization of the cranial and intracranial arteries and veins by the injection of a radiopaque material. It is the purpose of this presentation to describe the technique for precision visualization of the intracranial arteries and veins by making the injection through a polyethylene tube which has been threaded through a needle into the vessel. The instillation of radiopaque contrast media inside a cerebral vessel through a plastic tubing, by percutaneous needle puncture, appears to have certain distinct advantages over the commonly used needle puncture technique. Chief among these is elimination of trauma to the vessel lining by movement of the sharp needle within the vessel lumen. Any decrease in intimal damage will undoubtedly lessen the hazard from traumatic thrombi and emboli. Again, once the tubing is in place the procedure may be carried through with the necessary deliberation for proper positioning of the head and the making of any number of exposures that may be required to precisely visualize the lesion.

The method is applicable to visualization of the common carotid and vertebral arteries and their branches, the cerebral veins, the dural sinuses, jugular vein, and even other vessels of the body.

The following technical details are supplied as the *sine qua non* of this particular, proved method of obtaining good results, even though other methods are commonly in use.

INJECTION EQUIPMENT

A successful study depends more upon adequate equipment in proper condition than upon the skill of the operator. After establishing the correct technique and preparing the exact equipment necessary we have observed excellent results even in the hands of a novice.

1. *Needle* (Fig. 1). This basic item must be of stainless steel. It should be 3 inches long, Luer-Lok, with a fitted stylet like a spinal puncture needle. The function of this stylet is to protect the needle lumen from foreign particles during storage. The diameter is 16 gauge, made from special, thin-walled tubing. This enlarges the lumen to that of a 15 gauge needle, in order to accommodate plastic tubing of sufficient caliber to simulate an injection through an 18 gauge needle, and yet reduce the outside diameter of the needle to an absolute minimum. The bevel length should be 5 mm. so as to form an angle of 10 degrees with the longitudinal axis of the needle. The shaft must not be swaged to the hub (as is customary) but must be externally soldered to prevent any reduction in the lumen at the junction.* The transition area from hub to shaft should be smoothly funnel-shaped to facilitate the passage of the plastic tubing through it.

Of great importance is the maintenance of an exceedingly sharp needle point. It is best to sharpen the point on a hard slip stone before each usage, and according to the technique published in a pamphlet on sharpening needles, obtained also from Becton, Dickinson and Company. The back, inside edge of the bevel must be dulled to prevent the cutting of a biopsy plug from the artery. This is done by charging a length of hard twine by pulling it

* Such a needle may be obtained from Becton, Dickinson and Company, Rutherford, N. J., and is listed as Special Needle No. T 462LNR, 3 inches, 16 gauge, 5 mm. bevel.

* Grateful acknowledgment is herewith made to Paul C. Swenson, M.D., Professor of Radiology at Jefferson Medical College and Hospital, for the kind cooperation and advice from his department in performing arteriography and preparing this report.

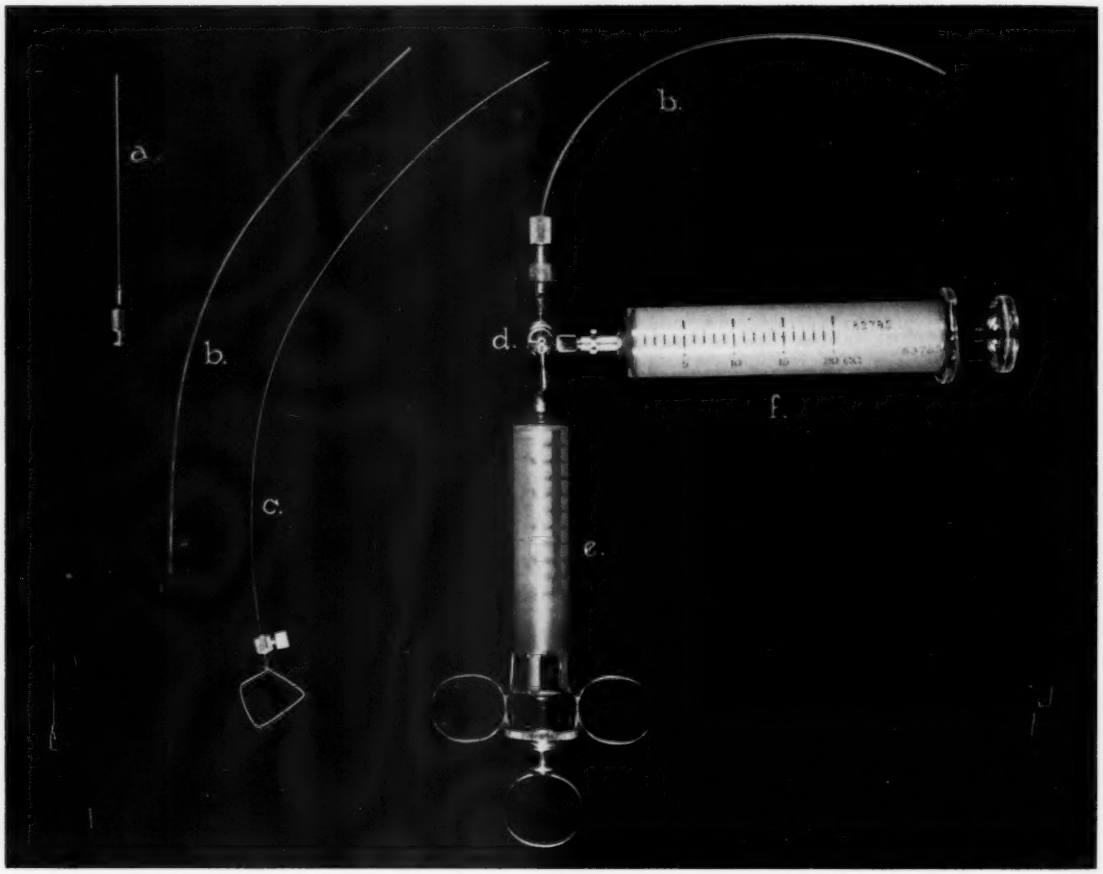

FIG. 1. Apparatus for arteriography. *a*, special needle for carotid puncture; *b*, polyethylene tubing; *c*, stylet for inside tubing and also the measuring guide; *d*, three-way stopcock; *e*, pressure-exerting type of syringe; *f*, salt solution syringe. (Reproduced by permission of *Surgical Clinics of North America*, 1952, *32*, 1575.)

through a stick of red rouge of medium grit. The twine is then pulled out the point end of the needle, keeping it taut and almost perpendicular to the needle axis so as to blunt the sharp back edge of the bevel. The edge can also be removed by a sharp cutting tool. The point is protected during storage and sterilization by sheathing it in a short length of plastic tubing or else the wire insulation ("spaghetti") obtainable in any radio parts store.

An additional stylet should be fashioned (and rouge polished) from stainless steel, type 302, spring tempered wire* of 0.051 inch gauge. As indicated in Figure 1, this stylet is 4 mm. longer than the needle and the point end curves gently so as to efface the sharp needle point when the stylet is properly oriented within the needle. This serves to prevent intimal damage when the needle is advanced up the artery prior to inserting the plastic tubing.

Some sort of hollow handle is needed with which to hold and manipulate the needle while performing the puncture. We commonly employ a 5 cc. Luer-Lok glass syringe.

2. *Plastic Tubing.* Either boilable, vinyl plastic tubing or the polyethylene variety may be used. We use the latter of 0.050 inch outside diameter, 0.034 inch inside diameter, and in 22 cm. length. Unfortunately, the caliber of this kind of tubing varies from lot to lot. Sometimes it will pass readily through the needle, and sometimes it is oversize and must be stretched to re-

* Obtainable from Alloy Metal Wire Co., Prospect Park, Pa.

duce its caliber. Stretching is accomplished by applying hemostats to the ends of the tubing, immersing this in boiling water for thirty seconds, and then immediately stretching the piece (over the gauge wire described below) so as to increase its length by 10 to 15 per cent. The stretch limit is that which falls just short of producing undulations in the long axis of the tubing. While maintaining the tubing taut it is plunged into cold water for fifteen seconds, and is then cut to size, being careful to eliminate the distorted ends. Consistency in length and inside diameter is maintained by internally gauging each piece with a stainless steel, rouge-polished, type 302 spring-tempered wire of 0.030 inch gauge fashioned as in the diagram, and 24 cm. long. The sliding stop can be made from a female, brass binding post of the screw (not spring) vise type obtainable in any radio parts store. This gauge wire is kept sterile during arteriography in order to estimate externally where the tip of the tubing lies in the artery.

3. *Tubing Adapter.* The polyethylene tubing is connected to the syringes via a Touhey spinal catheter adapter which is soldered to the male end of a three-way stopcock.* Since the 0.050 inch tubing is somewhat smaller than the ureteral catheter used for continuous spinal anesthesia the rubber collar in the squeeze-joint of the adapter must be replaced by a thicker wall collar. This is the best cut to the proper length out of white rubber uterine supporter tubing (1/16 inch inside diameter and 7/128 inch wall). The two female ends of the three-way stopcock should be Luer-Lok.

4. *Syringes.* The syringe used for the contrast medium should be a 10 cc., Luer-Lok, three-ring type. This has proved best for making the injections at the optimum speed, meaning as fast as possible, through such a syringe. It is attached to the arm of the stop-cock in line with the plastic tubing. To the sidearm is attached the second syringe, containing the solution used to prevent clotting and keep the system open. A 10 cc. or 20 cc. Luer-Lok syringe is adequate if physiologic saline solution is to be used. However, if citrate or heparin solutions are employed a 5 cc. syringe should be used to minimize the amounts injected. Such can be facilitated by plugging up the metal tip of the syringe with solder into which a short piece of a hypodermic needle shaft (25 gauge) has been fixed to decrease the caliber of the orifice.

5. *Solutions.* Since the catheter method safeguards against extravascular injection, one of the chief disadvantages of thorotrast (25 per cent colloidal suspension of thorium dioxide) is therefore overcome. We have preferred this medium, furthermore, because: it is seldom necessary to use more than 30 cc. to complete a study; the chances of future radioactive complications are negligible; the injection is completely painless; the density of the contrast shadow is slightly greater than with the usual iodinated compounds; the immediate, toxic reactions are probably less than with such compounds; and there is no sensitivity problem. However, in the very young age group we consider 35 per cent diodrast to be preferable, although sodium pentothal anesthesia is necessary in many cases to guarantee against movement of the patient during exposure.

Since the solutions are already sterile it is only necessary to immerse the vials or ampules in 70 per cent alcohol for ease in handling by the sterile assistant.

If physiologic saline solution (or isotonic sodium citrate) is used to rinse equipment and to prevent clotting it *must* be prepared in such a way that no lint from filters and no particulate matter whatsoever be permitted to contaminate it. Certainly it should be processed through porcelain filters in order to obviate embolic phenomena. It should be supplied in 100 cc. vials, or less, and the syringes should be filled directly from these vials.

6. *Sterilization and Surigcal Set-Up.* Except for the solution and the syringes (heat

* Becton, Dickinson: L/S2 or 5031/S, depending on the handedness of the surgeon.

FIG. 2. Angioseriographic apparatus with electronic timer switches.

sterilized) all the equipment mentioned so far may be sterilized by immersion in 1:1000 aqueous solution of zephiran chloride. The catheters must also be perfused with the antiseptic. Precautions should be taken to thoroughly rinse the antiseptic out of the equipment with saline solution just prior to use. Before use the catheter is soaked for twelve to twenty-four hours in sodium citrate solution to discourage clotting on the outer wall.

In view of the fact that percutaneous injection is not 100 per cent successful and that, at times, it is more desirable to surgically expose the carotid vessels it is important to have an appropriate, surgical set-up available and open when the test is begun. This means that all the instruments necessary, plus the electrocoagulating unit, suction apparatus, and adequate lighting are to be prepared. This implies the absolute necessity of arranging for an adequate number of personnel, meaning one assistant and at least one nurse in addition to the personnel of the roentgen department. Many of our difficulties in the past may be traced to poor preparation, inadequate equipment, and insufficient personnel. Arteriography is an exacting, often time-consuming procedure, which must be done with great precision, accurate timing, and respectful caution. In these respects it differs from other, less complicated, neurosurgical contrast studies.

ROENTGENOGRAPHIC EQUIPMENT AND EXPOSURE FACTORS

This equipment must satisfy certain specifications: maneuverability, synchronization, stereoscopy, seriography, and the capacity to produce roentgenograms of great clarity. At present we have not found it possible to realize all these objectives in one piece of equipment. We therefore employ two major items. The first is a roentgenographic head stand with a Potter-Bucky diaphragm (6:1 grid) and a fixed target to film distance of 36 inches. The tube and Potter-Bucky diaphragm can be rotated through 360 degree arcs in both vertical and horizontal directions. An adequate compression band and head clamp are included to immobilize the head during exposure. The tube is a regular rotating anode type with a 2 mm. focal spot requiring a 200 ma. control with four valve, full wave rectification. Tube capacity is 100 kv. (peak). Merely to suggest a base line the following exposure factors are given in the technique for an average adult (10 by 12 inch film):

1. Anteroposterior projection: coned, 70 kv., 200 ma., $\frac{1}{2}$ second, 36 inches. 2. Lateral projection (stereoscopic): coned, 70 kv., 200 ma., $\frac{1}{4}$ second, 36 inches.

For seriography we use a custom-made, angioseriographic device with an electronic, automatic timer allowing eight exposures over a twelve second period, with the capacity for timing at varying intervals (Fig. 2). The cassette trays are fastened to a continuous chain moving in a horizontal

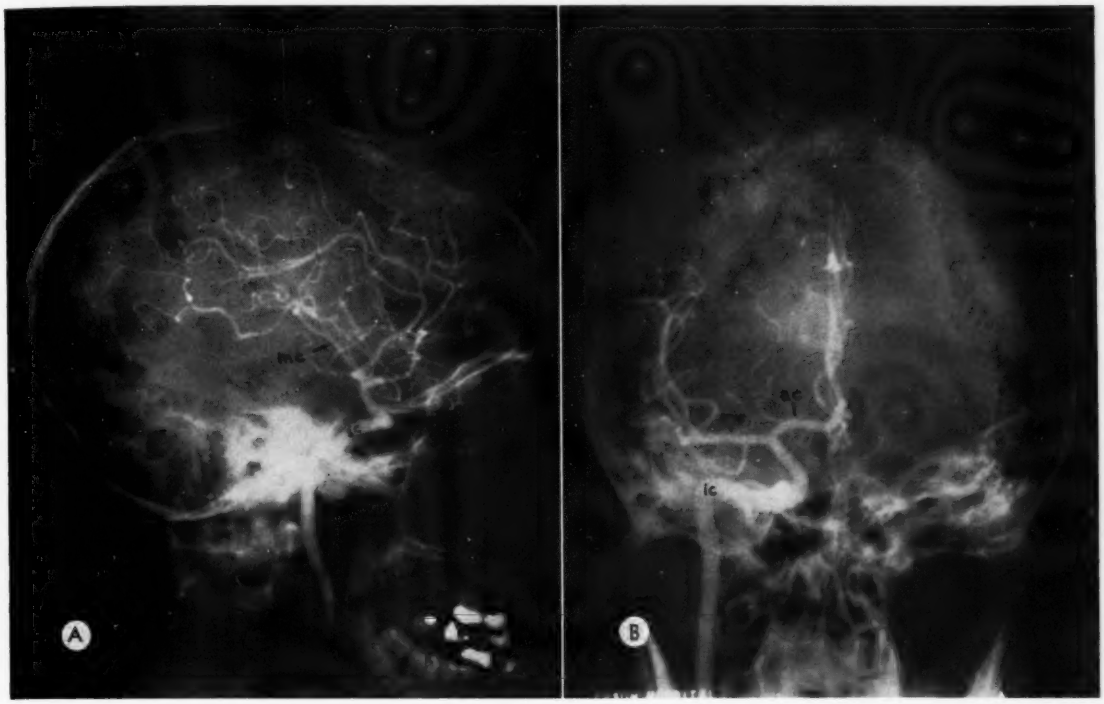

Fig. 3*A*. Normal, lateral projection carotid arteriogram (thorotrast). *ac*, anterior cerebral artery; *mc*, middle cerebral artery; *ic*, internal carotid artery.
Fig. 3*B*. Normal anteroposterior projection. Note filling of both anterior cerebral branches.

plane. The film size is usually 8 by 10 inches, but films up to 11 by 14 inches can be accommodated. We employ a cross-hatch grid which is fastened to the bakelite surface of the film cabinet, *i.e.*, the exposure area. The tube standard is floor mounted on a monorail. The tube itself is a special, heavy duty, rotating anode type requiring a 500 ma. control with four valve, full wave rectification. Tube capacity is 120 kv. (peak). The head is manually immobilized by an assistant during exposures. The technique for the average adult is: 1. Anteroposterior projection: coned, 95 kv., 300 ma., 1/8 second, 36 inches. 2. Lateral projection (stereoscopic): coned, 95 kv., 300 ma., 1/20 second, 36 inches.

In setting up control devices for any arteriographic equipment it is necessary to provide two separate switches: one to initiate anode rotation, and one to make the exposure instantly at the command of the surgeon.

An essential item is the chair or table on which the patient lies. This must be sufficiently adjustable to fulfill three requirements: the proper height to conform to the operator's comfort, the proper extension of the head to stretch out the carotid artery and facilitate puncture of that vessel, the proper flexion of the head and neck to procure the difficult anteroposterior projection film. This must be taken so that the basal portions of the anterior and middle cerebral arteries as well as the intracranial carotid artery are projected clear of (*i.e.*, above) the frontal sinuses; to accomplish this the orbits must be superimposed over the petrous pyramids. This can be achieved only by combining a horizontal tilt of the Potter-Bucky diaphragm (with the caudal edge downwards) to about 18 degrees in the average case with extreme flexion of the neck, trying to fix the chin on the chest. Perhaps the tube must be tilted contrariwise when the patient has a short neck or a stiff neck. The

Fig. 4*A*. Lateral projection of normal vertebral arteriogram. *v*, vertebral artery; *b*, basilar artery; *pc*, posterior cerebral arteries. (Reproduced by permission of *Surgical Clinics of North America*, 1952, *32*, 1578.)
Fig. 4*B*. Anteroposterior projection. The arteries are more tortuous than in a younger person. (Reproduced by permission of *Surgical Clinics of North America*, 1952, *32*, 1578).

best type of apparatus to fulfill these requirements is a dental chair which can be raised and lowered hydraulically, whose seat and back rest can be levelled off and also tilted backwards. This item is even more essential in the angioseriographic apparatus which does not have the tube and cassette adjustments of the roentgenographic head stand. Furthermore, the dental chair should have a removable head rest which is never needed, a footboard to prevent the patient from sliding down out of position, and arms which can be removed to facilitate transfer of the patient off and on to his stretcher and simply because they encumber the operator and his assistant.

Finally, it is desirable to strap the patient's thighs and ankles, and apply wrist straps as during any surgical procedure to eliminate interference with the operation as well as to immobilize the patient during the exposure.

VESSEL PUNCTURE AND INJECTION TECHNIQUE

There are two ways to percutaneously puncture the carotid artery. The first is the hit-or-miss stab technique advocated by the bold or careless surgeon who is indifferent to tissue damage or who does not comprehend the gravity of unnecessary intimal trauma with resultant embolic complications or a preventable hematoma in the neck. The second method is the meticulous, deliberate approach wherein the surgeon is constantly mindful of such complications.

It is essential first to prepare the patient; this means closely shaving both sides of the neck, and giving sufficient barbiturate, atropine and morphine to render the patient fully cooperative. In the agitated patient or when diodrast is used, a general anesthetic is desirable; the best is intravenous sodium pentothal. Diodrast sen-

sitivity testing should be done before the patient is medicated.

After properly positioning the patient, as previously described, it is best to raise him up to stretch out the carotid vessel. Sometimes it is necessary to let the head hang back almost free of the roentgenographic table. If right handed, the operator assumes a position on the patient's right side, regardless of the side of injection. Then, a small amount of 1 per cent procaine is injected in and beneath the proposed site of skin puncture. It is very important not to so flood the area as to obliterate landmarks and vessel pulsation, but it is desirable to inject enough anesthetic beneath the carotid sheath to try to produce paralysis of the periarterial sympathetic nerves. All this can be accomplished with less than 5 cc. of solution. A similar injection should be made into the site of entry of the spinal accessory nerve into the sternocleidomastoid muscle to reduce tension thereof and increase the palpability of the carotid vessel.

By this time sedation or anesthesia may have so lowered the systemic blood pressure that carotid pulsation has become scarcely discernible; and the force of the pulsation is also decreased by excessive extension of the head (an obvious disadvantage of this position). One can correct this situation

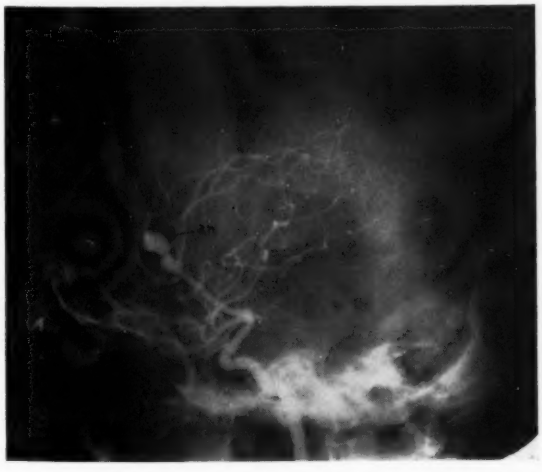

Fig. 5. *an*, saccular aneurysm arising from anterior cerebral artery (*ac*). Clipped surgically with good result.

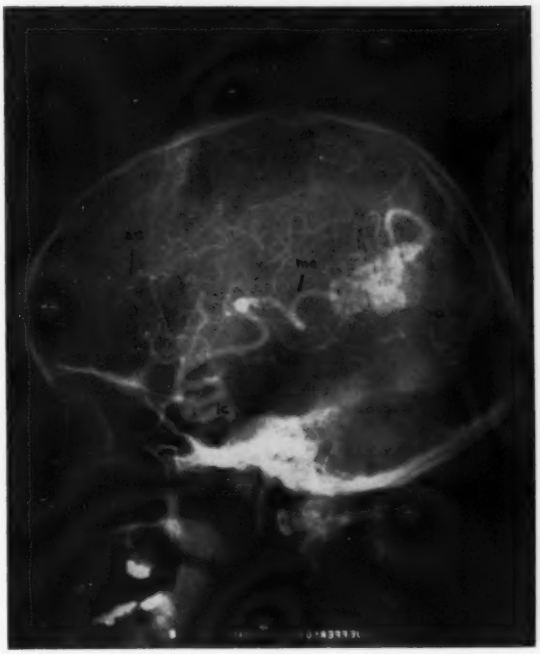

Fig. 6. *ava*, arteriovenous angioma of left cerebral hemisphere; *mc*, huge, dilated middle cerebral artery feeding the lesion; *ic*, internal carotid artery; *ac*, anterior cerebral artery. Angioma was removed surgically with good recovery.

by an intravenous injection of a vasoconstricting, vasopressor drug such as 1:1000 adrenalin or ephedrine sulfate. Very small amounts (such as 0.2-0.3 cc. of the former or 25 mg. of the latter) are sufficient, and even these may cause intense headache for about five minutes. There is an immediate intensification of the carotid pulse.

Clearly, it is desirable to puncture the common rather than the internal carotid artery to avoid unnecessary damage to the latter. Still, there are two sites of puncture: one is just above the clavicle and the other is just beneath the carotid fork. The former has the advantage of permitting a very oblique course of the needle through the superficial tissues and the artery itself. This minimizes postoperative leakage, and increases the length of tubing within the artery, safeguarding against inadvertent extraction of the tubing when the head is turned laterally. The second site of puncture permits a greater possibility of guiding the tubing directly up into the internal branch,

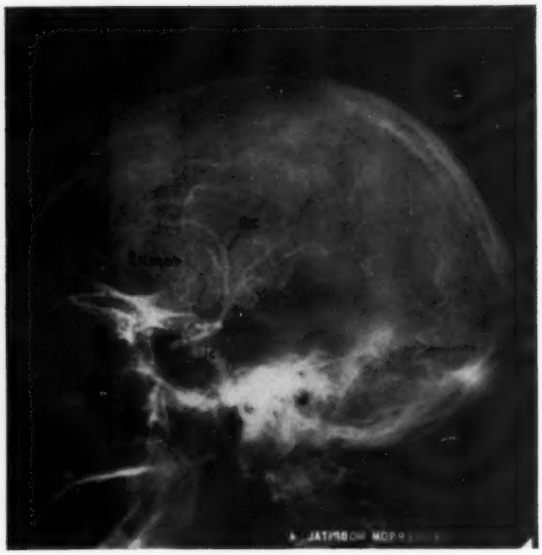

FIG. 7. Severe, posterior displacement of anterior cerebral arteries (*ac*) by cribriform plate meningioma, completely removed by craniotomy; *ic*, internal carotid artery.

which obviously improves the clarity and density of the intracranial vessels on the film. This is facilitated by first inserting the curved tip stylet into the needle after the artery has been entered, thence advancing the needle up into the internal branch without damaging the intima. Another maneuver, when using the lower puncture site or when not using the stylet, is digital occlusion of the external branch to force the blood supply through the internal branch, thus influencing the passage of the catheter up the latter course. Conversely, it is possible to occlude the internal branch in studying the extracerebral vessels.

One indication that the catheter has passed up the internal branch is the production of orbital or retro-orbital burning pain following the rapid injection of 1 or 2 cc. of isotonic sodium citrate solution. This pain will appear elsewhere on the face or head or in the mouth if the catheter is in the external branch.

The 5 cc. syringe attached to the needle, and containing 1 cc. of saline solution, is held somewhat like an orchestral baton or fencing foil with three fingers beneath and the thumb above. After making a 1/4 inch stab incision through the skin, to minimize needle blunting, the needle is advanced, bevel up, until it rests against the artery, as indicated by the transmitted pulsations. The adventitial coat is lifted on the tip of the needle which is then slowly advanced obliquely upward into the lumen. When successful, pulsating arterial blood will shoot back into the syringe. If the needle is in the jugular vein the blood will be darker, there will usually be no pulsations, and the blood can be sucked back into the vein by a deep inspiration. Then, using the maneuvers previously mentioned, the polyethylene catheter is passed through the needle into the artery, finally withdrawing the needle. Immediately the Touhey adapter stopcock must be attached and irrigation begun to avoid clotting. After passing the tubing up into the internal branch, only about 2 or 3 inches should remain in view. After positioning the head for the anteroposterior film, as discussed already, a trial injection is made with saline through the same 10 cc. Luer-Lok syringe to be used for the injection of the contrast medium. This is exceedingly important in order to properly adjust the screw-cap of the adapter: if the squeeze joint is too tight, the injection will be too slow; if the joint is too

FIG. 8. Falx meningioma (*m*) involving the superior longitudinal sinus. This is a late arterial phase, seriographic exposure demonstrating extensive filling of a very angioplastic tumor.

loose, there will be leakage or perhaps the catheter will be exploded out of the adapter. Since the first injection of the medium is actually a survey film to determine which vessel has been entered, it is wise to use the anteroposterior projection, for stereoscopy is not important here, and the survey film may be sufficient to fulfill the anteroposterior requirement. This helps reduce the total amount of thorotrast. Six cubic centimeter amounts are usually appropriate for all injections.

For perfect synchronization the following step-by-step procedure is advocated:

1. The operator himself ascertains the proper positioning of the head, attaches the Luer-Lok syringe for the contrast medium and so holds this that his dominant thumb is in the end ring and his index and middle fingers are outside instead of within the side rings. This increases his purchase and therefore the force and speed of the injection which must be made as rapidly as possible. He thoroughly lubricates the exposed shaft of the piston with saline solution, and this is most important for diodrast. He then digitally occludes the opposite internal carotid artery to assure anterior cerebral filling.

2. His first command to the roentgen technician is, "Are you ready?" If she replies in the affirmative,

3. his next command is "Get ready." She then initiates rotation of the tube anode and the assistant automatically turns the stopcock orienting the contrast medium syringe with the catheter.

4. Allowing about five seconds for anode rotation to reach its peak speed the operator, still occluding the opposite carotid artery, rapidly injects the contrast medium, and commands, in a loud voice, "Shoot!" just as 5 cc. have gone in. This allows for the lag produced by the human element in receiving and effecting the command, as well as by the inertia of the Bucky diaphragm. At this third command the technician instantaneously makes contact for exposure. In the roentgenographic head stand this serves both to start the Bucky

Fig. 9. Superior longitudinal sinus angiogram in the meningioma case illustrated in Figure 8. This demonstrates that the tumor has completely occluded the sinus, thus eliminating any risk in surgically resecting this important structure. *sls*, superior longitudinal sinus; *ts*, transverse sinuses; *ss*, sigmoid sinus; *t*, trephine hole where polyethylene tubing enters the sinus; *p*, posterior limit of occlusion of sinus by the tumor.

apparatus and fire the tube. In the angioseriographic apparatus exposures and travel of the cassette belt are both initiated by one contact. The number of exposures and intervals between are variable and predetermined before each series by adjusting the electronic timer.

5. After the exposure the assistant turns his irrigating syringe into the circuit, slowly maintaining an open system.

6. While waiting for film development the operator or his assistant should check the patient for complications such as: extravasation of blood around the catheter (treated by digital compression), focal palsies, convulsions, or hyperemia of the skin or conjunctiva. During this interval the patient's strained position can be relaxed by releasing the head clamp and raising the patient. If significant neurologic complications occur, it is sometimes wiser to abandon the procedure.

The developed film is then inspected. It may be unsatisfactory for several reasons: movement of the patient, poor positioning, poor synchronization, technical failures of the roentgenographic equipment or film de-

velopment, a prolonged injection, breakdown of the injection equipment, or injection solely or partially into the external carotid system. Only this last most common cause need be considered since corrections of the others are obvious. Frequently it is impossible to pass the catheter into the internal branch but the disseminated filling due to a common carotid injection may be satisfactory anyway. However, if the catheter went up into the external branch it must be cautiously withdrawn so that its tip lies just beneath the fork. This is determined by externally aligning the gauge wire with the catheter, setting the tip of the former at the skin landmark just beneath the fork, and then withdrawing the catheter to that point. The injection is then repeated until the desired result is obtained.

Routinely, the stereoscopic lateral pair of films is then made with two similar injections. The ipsilateral side of the head is turned down against the film, which may require slight rotation of the patient's body and elevation of the opposite shoulder by a sandbag. In this position it is difficult to palpate the opposite carotid artery (being obliterated by the sternocleidomastoid muscle) but approximate digital compression is applied. One should be certain of two factors: the head must be held rigidly by either a compression band or an assistant to prevent change of position between the two exposures; since the length of the route from skin to carotid artery is increased when the head is so rotated, it is possible for the catheter to slip out of the artery unless it is well inside. Under optimum conditions a minimum of three films and 18 cc. of thorotrast are required for a satisfactory study, unless some situation is present as will be discussed later under modifications in technique.

Arteriography of the vessels in the posterior fossa or of the occipital lobes is performed by injecting the contrast medium by the same technique into a vertebral artery where it enters its foramen in the transverse process of the sixth cervical vertebra. Either vertebral artery may be selected since both contribute equally to filling of the basilar and posterior cerebral arteries. The exposures are the same as for the carotid study. In view of the small caliber of the vertebral artery it would be advisable to use the next smaller gauge needle with appropriate sized catheter.

Finally, at the end of the procedure, the catheter is withdrawn and digital compression is maintained for five minutes against the site of arterial (not skin) puncture to prevent a hematoma. Despite this precaution this may occur in the following minutes or hours and may require surgical evacuation if respiratory distress develops from tracheal compression.

This same catheter technique is also applicable to superior longitudinal sinus angiography, a procedure necessary to demonstrate thrombosis or neoplastic occlusion of the dural, venous sinuses. A trephine hole is made over the pre-rolandic section of the sagittal sinus. A tiny nick is made, precisely in the mid-sagittal line, into the sinus, to permit retrograde insertion of the polyethylene catheter, *i.e.*, in an anterior direction. Diodrast injections are not painful as in arterial injections, making this medium the one of choice. Two precautions are necessary, as we have already sadly discovered, in order to prevent extravasations of the irritating diodrast into the subdural or subarachnoid spaces. The catheter should not be advanced more than 1 cm. into the sinus to prevent its passage out into a cerebral vein. Secondly, just in case this did happen, the injection should be made slowly, using about five seconds to inject 10 cc. of the medium, to prevent rupture of a vein. Slight obliquity of all projections is necessary to better visualize the sinuses.

It is obvious that there is a most definite requirement for success: an alert, practiced team.

PRECAUTIONS TO BE OBSERVED WITH THE INJECTIONS AND EXPOSURES

Contrary to the similarity from case to case in other neurosurgical contrast studies, arteriography demands a more careful analysis of each patient's problem.

Before answering certain questions we must be mindful of three items:

1. This is a potentially hazardous procedure and the surgeon should be ever conservative, never subjecting the patient to unnecessary risks by inappropriate or excessive injections.

2. Thorotrast, a radioactive substance, has potential, carcinogenic properties and the total quantity used should be limited. Unfortunately, we do not actually know what is the maximum limit of safety and have only theoretical standards available. Certainly there are exceedingly few case reports in the literature about known malignancy resulting from the use of this agent. Perhaps a sufficiently prolonged time has not elapsed to permit such occurrences. Furthermore, as the life span continues to increase the consequences may become, theoretically, more important.

3. Excessive radiation is a hazard both locally and systemically for the patient and the personnel. However, we have measured the amount of radiation delivered to the hands and various other parts of the operator's body. This has demonstrated that one operator, of average sensitivity, under the conditions of our particular technique, can tolerate about 45 exposures weekly in order not to exceed the 1952 National Bureau of Standards' recommendation of 300 milliroentgens per week. We have not found it necessary to protect the operator or assistant with lead shields, although it is convenient and desirable for anyone who holds the patient's head to wear lead gloves and lead apron. Actually this unskilled task can be assumed by almost anyone, and therefore the same person need not be continually exposed. The hand which compresses the opposite carotid is most subject to undesirable radiation; this duty should be delegated to the assistant.

MODIFICATIONS IN THE TECHNIQUE OF ANGIOGRAPHY

1. Which contrast medium should be used? The advantages of thorotrast make it the most desirable medium presently available. However, when large amounts of medium are occasioned by special needs, or when there have been repeated failures due to technical difficulties previously mentioned, then 35 per cent diodrast should be chosen or substituted later.

2. Are seriograms necessary? Certainly there is no need in routinely using these for aneurysms of the circle of Willis, for cervical carotid occlusion, or for mass lesions whose essential characteristics are their size and location (*e.g.*, subdural hematoma). For such lesions it is far more important to have clear films obtained through a Potter-Bucky grid. We have frequently noted that the neurologist is interested merely in diagnosis; the surgeon needs additional information to plan his attack on the lesion. Even distal lesions such as arteriovenous angiomas seldom require seriography since the venous elements fill immediately. However, meningiomas are frequently best demonstrated in the venous phase and this is the chief indication for seriograms.

3. Is a delayed exposure ever necessary? Yes, under two conditions. First, one may be more interested in the distal than the proximal vessels and could profitably delay the exposure for a brief instant after all the contrast medium has been injected. Secondly, we have occasionally observed arrest in the progress of the medium so that the same phase has been present in all three or four films on a seriographic run lasting five or six seconds. This may have been due to arteriospasm. Repeat injections were necessary, delaying the exposure to obtain films of later phases.

4. Are larger quantities of contrast medium ever necessary? Yes, under four circumstances, 10-12 cc. should be used. The first two conditions are similar to those mentioned in the previous section; third, in case so much contrast medium is entering the external system that adequate intracranial filling is impossible with the 6 cc. injection; fourth, in the patient with extremely large caliber or tortuous vessels preventing good filling similarly.

5. When is it desirable to study the ex-

ternal carotid system? Vascular anomalies of the scalp and cranium, and meningiomas which may be supplied mainly by the middle meningeal artery are the chief indications.

6. Is the lesion in the cervical portion of the carotid artery? Many instances of cerebral thrombosis, so-called, are actually due to thrombotic occlusion of the first inch of the internal carotid artery. This has been repeatedly demonstrated by arteriography and confirmed surgically. In case intracranial filling is not obtained, and such a diagnosis is possible, the patient should be shifted upward on the film to obtain a view of the cervical carotid tree.

7. Is it always desirable to occlude the opposite carotid? No, there are three instances when this would be undesirable or even hazardous. First, when the involved carotid is pathologically occluded; second, when the cerebral blood flow is shunted out through a carotid-cavernous fistula; third, when the anteroposterior film demonstrated bilateral, middle cerebral filling; here, continuation of contralateral occlusion during the lateral projections enhances bilateral filling of so many vessels that it is difficult to distinguish between them, even stereoroentgenographically.

8. Is it just as or even more necessary to study the circulation on the uninvolved side? Yes, when an estimate of the collateral circulation through the circle must be made. This is particularly true in the presence of a carotid-cavernous fistula. In the 12 such cases in our own experience no patient had a hemiplegia unless the involved carotid was surgically occluded. This means that either collateral circulation from the opposite side was adequate or only a partial shunt was present. The former situation can be determined by injecting the opposite carotid, thereby suggesting that sometimes such a lesion should be treated by clipping the internal carotid first intracranially, and later in the neck.

9. Are special views ever necessary? Occasionally it is essential to take oblique views to better delineate an obscure lesion. This is especially true in aneurysms of the horizontal part of the anterior cerebral artery. These are best portrayed by rotating the head, and directing the roentgen-ray beam through the contralateral orbit and the ipsilateral occiput in the otherwise anteroposterior projection.

ADVANTAGES OF CATHETER TECHNIQUE

Since the polyethylene catheter is the outstanding difference between this technique and others we would attribute most of the advantages to it. They are as follows:

1. Accidental, extravascular injection is obviated, thus making thorotrast a more desirable medium since there is no danger of producing chronic granulomas in the neck.

2. Mechanical damage to the intimal lining of the artery is prevented, reducing complications due to embolic phenomena.

3. Precise, isolated injection of the internal carotid artery is facilitated without actually puncturing that vessel. This in turn reduces the total amount of contrast medium required, again contributing to the desirability of thorotrast.

4. The flexibility of the system eliminates the nervous strain and tension caused by trying to maintain a sharp needle immobile within the artery.

5. Maneuverability of the patient is assured for proper positioning without dislodging a needle in a precarious location. This eliminates the need for using special, vertical cassette holders with grids, with inferior results.

6. A more leisurely, accurate study is possible since the catheter may be kept in the artery relatively indefinitely, until the films are thoroughly inspected and decisions made regarding further exposures or special views.

SUMMARY

We believe that angiography performed through a plastic tubing inserted into the lumen of the vessel will result in film contrast of a superior quality to the other

techniques in common use. This method may be used to advantage in those instances where inadequate clarity by the rapid survey film technique, using the Fairchild photographic camera, necessitates more precise information for highly technical surgical maneuvers. With reasonable attention to all aspects of the hazards of intravascular manipulations and drug irritation the procedure carries risks that are minimal in terms of the seriousness of the disorders for which it is indicated as a diagnostic tool. Diagnostic precision, such as is possible by this method, is absolutely necessary for the successful outcome of many intracranial operations and no stone should be left unturned in attempts to accomplish such an end.

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ARTERIOGRAPHIC ANATOMY OF THE ANTERIOR CHOROIDAL ARTERY*

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THE introduction of surgical occlusion of the anterior choroidal artery as an operative approach to the therapy of hyperkinetic disease has resulted in the necessity of more detailed knowledge of the surgical anatomy of this vessel. Although fairly adequate descriptions of the gross anatomy of the anterior choroidal artery have been elaborated, more specific, detailed information is desirable in order to facilitate the surgical approach to this vessel in individual cases. We have found that one valuable method of appraisal of the anatomy of this vessel is by means of cerebral arteriography. This paper summarizes our study of the arteriographic appearance of the anterior choroidal artery in 100 consecutive cerebral arteriograms.

Egas Moniz reported that the anterior choroidal artery is visualized in the cerebral anteriogram in 71 per cent of cases and that in 73 per cent it originates directly from the carotid siphon, while in 23 per cent it originates at the level of the origin of the sylvian group. According to Ecker, "as seen in the lateral arteriograms, the anterior choroidal artery goes inferiorly for about 5 mm. It then continues upward for 2 or 3 cm. in a gentle curve which is usually convex up." Considerably more anatomic data are obtainable from arteriographic visualization of this vessel.

Our primary interest was in determining the frequency with which satisfactory visualization of the anterior choroidal artery is obtained by arteriography, and in determining how accurately arteriograms can predict the anatomy of this vessel in individual cases. Variations of the mode of origin have been described in earlier studies, the most frequent of which consists in the origin of the anterior choroidal artery from the posterior communicating or middle cerebral artery. These and other significant variations have now been confirmed by one of us (I.S.C.) during intracranial exposures of this vessel. During the course of our surgical experiences it became obvious that the carotid arteriogram and evaluation of the anterior choroidal artery should be part of the routine examination of the patients to be submitted to the operation. Moreover, in several cases in which the occlusion of the artery was attempted by means of silver clips, negative results were encountered. Postoperative arteriograms in these cases demonstrated the artery to be patent. Therefore, postoperative arteriography is also considered to be indicated in most of these cases. We also hope that eventually the anatomic information obtained at operation can be correlated with the anatomical characteristics of the artery as determined from the arteriographic observation. Certain correlations in this regard have already been made in conjunction with this present investigation.

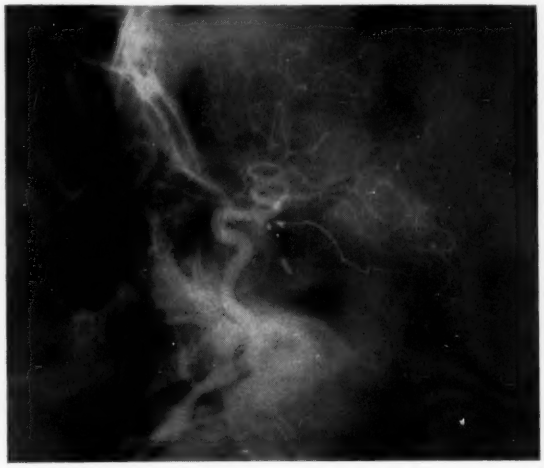

FIG. 1. Carotid arteriogram after attempted, unsuccessful surgical occlusion of the anterior choroidal artery. Note that the artery is patent. The arrow points to the silver clip. (Retouched)

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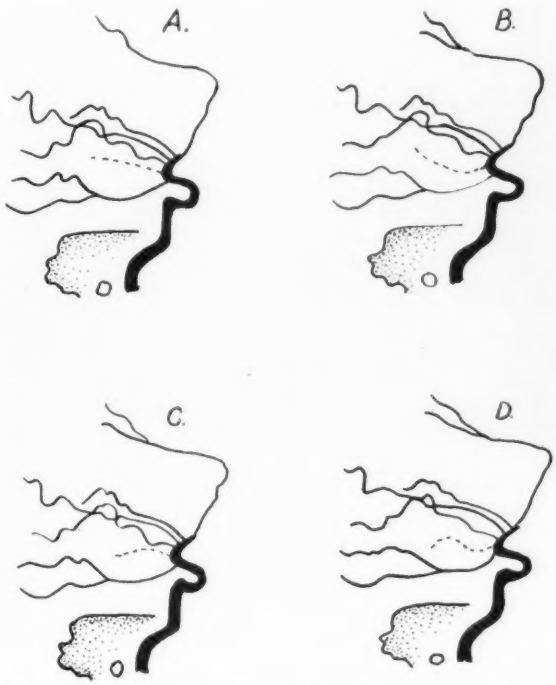

Fig. 2. Diagrammatic sketch representing the variation in the course of the anterior choroidal artery.

MATERIAL AND METHODS

One hundred normal lateral arteriograms were utilized for this study. The percutaneous technique was employed in all the cases. Diodrast was used in 92 cases and thorotrast in 8, both in amounts of 10 cc. The age of the patients ranged from seven months to seventy-eight years: 2 patients belonged to the age group 1–20; 41, to 21–40; 29, to 41–60; 9, to 61–80. The total number includes 9 cases in which arteriograms were performed bilaterally.

Fig. 4. Carotid arteriogram. The anterior choroidal artery describes a curve convex down. This type has been described as Type B. (Retouched)

The films were repeatedly and carefully examined. Consideration was given to the position, the course and the caliber of the artery as well as its topographical relationship to the point of bifurcation of the carotid artery and its relationship to the posterior communicating artery. In a few instances arteriography was combined with pneumocisternography to demonstrate the relationship of the vessel to the basilar cisterns. A classification was made according to the length of the vessel seen in the film, and each case was evaluated as "well

Fig. 3. Carotid arteriogram. The anterior choroidal artery, seen right above the posterior communicating artery, is of Type A. (Retouched)

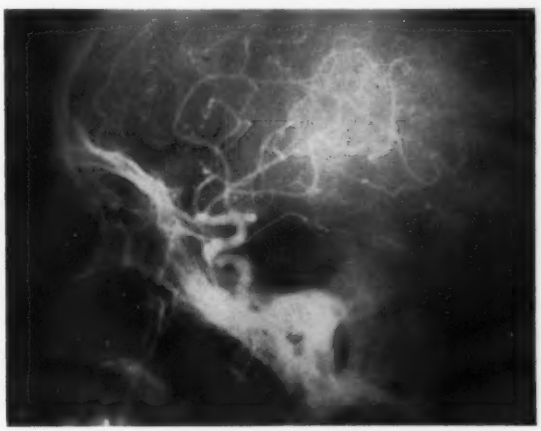

Fig. 5. Carotid arteriogram. The anterior choroidal artery is of Type C. The posterior communicating artery is not visualized. (Retouched)

FIG. 6. Carotid arteriogram. The anterior choroidal artery describes a double curve; Type D. (Retouched)

visualized," "fairly well visualized" or "poorly visualized" when the vessel, distinctly outlined, was seen, respectively, for a length of 4–5 cm., 3–4 cm., or 2 cm. In order to have comparative data, the posterior communicating artery was evaluated by the same criteria.

In this series the anterior choroidal artery was well visualized in 41 per cent of cases, fairly well visualized in 32 per cent, poorly visualized in 19 per cent, and not visualized in 8 per cent. The posterior communicating artery was well visualized in 37 cases, fairly well visualized in 16, and not visualized in 47. The course of the anterior choroidal artery was found to be variable and at least four different types were observed. These are schematically reproduced in Figure 2. The course was of Type A in 33 per cent, Type B in 20 per cent, Type C in 29 per cent, and Type D in 18 per cent. No significant differences in the various age groups were detected.

FIG. 7. Carotid arteriogram. The anterior choroidal artery and the posterior communicating artery are connected by a tiny vessel (arrow) which was distinctly seen at operation. (Retouched)

FIG. 8. Carotid arteriogram representing a situation similar to that described in Figure 7. The bridge-vessel is more evident. There was no operative control in this case. (Retouched)

The distance between the origin of the anterior choroidal artery and the point of bifurcation of the internal carotid artery varied between 1 mm. and 10 mm., with an average of 5 mm. The distance between the point of origin of the anterior choroidal artery and that of the posterior communicating artery ranged between 1 mm. and 6 mm., with an average of about 2 mm. The anterior choroidal artery was clearly seen to

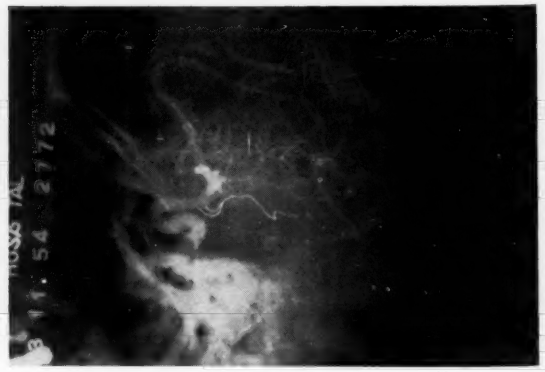

FIG. 9. Carotid arteriogram. Two small arteries join together to give origin to a main branch. These findings were confirmed at operation. (Retouched)

originate from the middle cerebral artery in 1 case and from the posterior communicating artery in 8 cases. The study of the 9 cases in which the arteriogram was performed bilaterally revealed varied differences between the two sides.

In 18 cases of this series, the arteriographic findings were checked at operation or by examination of the brains at necropsy. In 1 case only, the anterior choroidal artery was present and patent but could not be visualized in the arteriogram. In 1 case an anastomosis between the posterior communicating and anterior choroidal artery was seen at surgery. Re-examination of the preoperative arteriogram demonstrated this anastomosis. In another instance, the operative findings confirmed the arteriographic observation of two small arteries joining together to give origin to a main branch, from which the posterior communicating artery took origin. The latter was not visible in the arteriogram, although the anterior choroidal artery was well visualized. Obviously, it should always be kept in mind that arteriography can represent the anatomical situation only up to a certain degree, mostly because it lacks dimensional effect. However, considerable valuable and fairly detailed anatomic data can be obtained preoperatively by careful arteriography. The identification of the anterior choroidal artery is often made difficult by the branches of the middle cerebral artery. We have attempted to obviate this difficulty, resorting to two methods: (1) rotation of the head around the anteroposterior axis (chin away from the cassette), (2) injection of only 1–2 cc. of radiopaque medium. Figure 10 shows one of the films in which an elective visualization of the anterior choroidal artery and the choroid plexus was obtained by this method.

In conclusion, it can be said that the anterior choroidal artery is visualized in normal lateral arteriograms in 92 per cent of cases and that its point of origin is usually in the posterior aspect of the supraclinoid portion of the internal carotid artery, about 2 mm. above the origin of the posterior communicating artery and about 5 cm. below the bifurcation of the internal carotid artery.

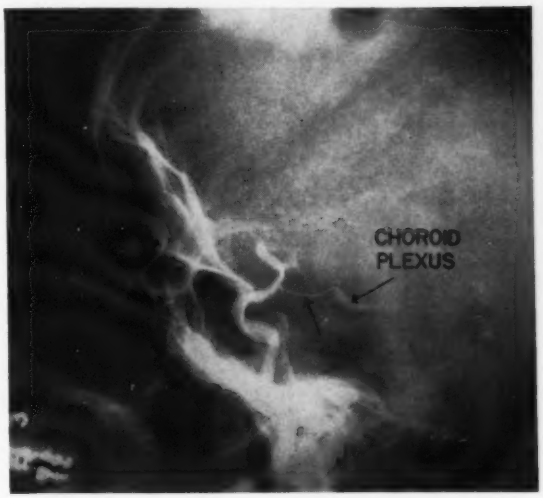

Fig. 10. Carotid arteriogram performed by injecting only 2 cc. of diodrast. Selective filling of the anterior choroidal artery (arrow) was obtained. Note also the distinct outline of the choroid plexus. (Retouched)

SUMMARY

The arteriographic anatomy of the anterior choroidal artery was studied in 100 normal cases. The anterior choroidal artery was visualized in 92 per cent of the cases. Its course appeared variable. The importance of the arteriographic studies before and after surgical occlusion of the anterior choroidal artery is emphasized.

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MARKED AORTIC CALCIFICATION IN A YOUNG WOMAN*†

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WE HAVE recently had as a patient in our hospital a young woman who showed, in view of her age, an unusual roentgen finding. Since we have not been able to find a similar case in the recent literature we assume that it is worthy of publication. The patient, thought by the medical department to have a congenital septal defect, presented on roentgenologic examination an aorta of extraordinarily small caliber which in the entire thoracic portion was converted into a calcified tube. Exploration was refused and therefore the clinical diagnosis cannot be corroborated. This is, however, of minor importance in this communication where interest is centered on the monstrous calcification.

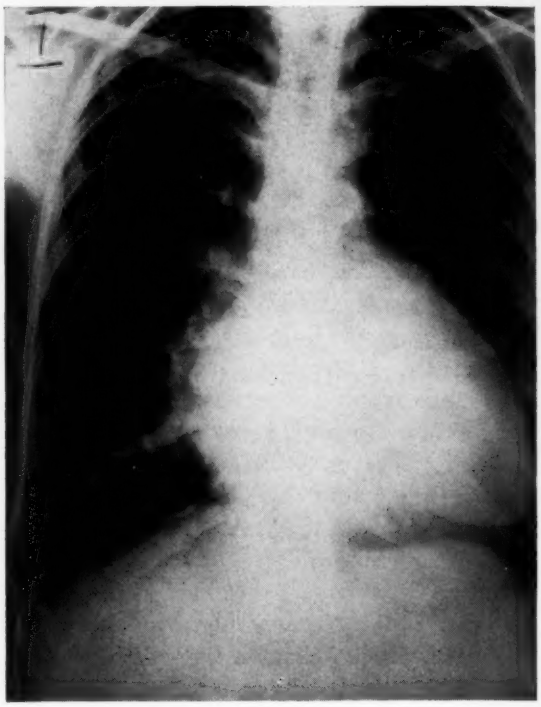

Fig. 1.

REPORT OF CASE

The patient was a woman, aged twenty-five. The parents and one brother are normally developed. The mother was well during the pregnancy and had no history of measles. The patient was a full term baby. At the age of two she had pneumonia and the doctor recorded that she had heart failure. Since then she had had numerous episodes of bronchitis. She has always been small in stature; her height at admission was 142 cm. She was a good student. She participated in games with other children, but at the age of fourteen she began to notice dyspnea and palpitation. Since August, 1949, she had felt tired and had had dyspnea, palpitation, vomiting and fever. In September, 1949, she had pneumonia and in the past year precordial pain and cough began and had become constant.

Examination on admission showed that the patient was small and well formed, with small hands and feet; she looked like a teen age girl. Her mentality was normal. There was considerable cyanosis of the cheeks, nose and ears. Slight ankle edema was present. Blood pressure in the right arm was 210/60, left arm 200/50, and in both lower extremities at the popliteal fossa the blood pressure was 190/80. She had bilateral cataracts. There was a loud systolic murmur with thrill heard in the second left interspace; P_2 was accentuated. The apex impulse was present in the anterior axillary line and there was normal rhythm.

The liver was palpable. The electrocardiogram showed right ventricular preponderance with a low ST in all leads. Hemoglobin was 70 per cent, red blood cells numbered 4,830,000, index was 0.7 and white blood cells numbered 7,185. The serum cholesterol was 136 mg. per 100 ml. The urine showed albumin and the Takata reaction was positive.

Roentgenograms showed well formed bones. Roentgen examination of the heart showed a cardiothoracic ratio of 15.5 to 24 cm. on a film taken at 2 meter focal film distance. The

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† Translated by Magnus I. Smedal, M.D., Boston, Massachusetts.

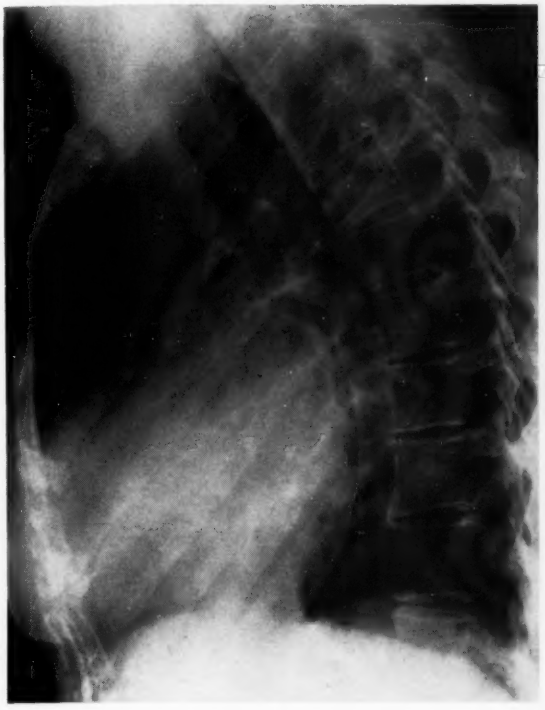

Fig. 2.

Fig. 3.

rhythm was regular; the pulsations were not unusually forceful roentgenoscopically. There were increased markings and hilar shadows characteristic of stasis. The pulmonary vessels did not pulsate abnormally. On the right side the costophrenic angle was obscured by a plate-like calcification which extended along the diaphragm, presumably an old pleuritis. The pulmonary conus was prominent. The right heart, both auricle and ventricle, was enlarged. An enlargement of the left ventricle and probably the left auricle was also present. The aortic window was not demarcated. The interventricular notch was not seen. The aorta was unusually calcified and it could be traced from the ostium down into the abdomen (Fig. 1, 2 and 3). The aortic arch did not have a rounded shape on the left side in the posteroanterior position. The caliber of the aorta was extraordinarily small throughout its course, and at the level of the diaphragm the diameter of the film was less than that of one's little finger.

The patient was afebrile except terminally when she also had constant tachycardia of 110 to 120. Toward the end she complained of precordial pain. At times she had dyspnea with increased cyanosis. Penicillin did not have any effect. She demanded discharge from the hospital against advice, and died at home the day following discharge.

DISCUSSION

A markedly calcified aorta is an unusual and peculiar occurrence at such a young age. A roentgenogram taken nine months before admission to this hospital showed the same degree of sclerosis. Calcification of the coronaries and other arteries without apparent cause has been seen in the newborn. Similar calcification in coronary arteries is seen in infants, in young people with diabetes or chronic nephritis. The pathogenesis in this case must be different. A hypoplastic aorta may be congenital but, on the other hand, it is usually seen with septal defects and it is explainable on the assumption that the left ventricle does not have sufficient blood volume with which to work. A septal defect will show or produce, in addition to physical underdevelopment, certain degrees of heart findings, cyanosis, right-sided preponderance

by the electrocardiogram, enlargement of the right heart, and there will be repeated attacks of bronchitis and bronchopneumonia. One can also postulate a possible combination of atrioseptal defect in congenital hypoplastic aorta. The pronounced sclerosis of the aorta in this case, on the other hand, can hardly be explained. The sclerosis of the hypoplastic aorta may possibly be a compensatory measure. The patient's hypertension must be explained on the basis of the sclerosis and cannot be a primary hypertension with secondary arteriosclerosis. Metabolic or endocrine disorders were not demonstrated and there were no hereditary factors involved. Serum cholesterol was normal. Meinicke's reaction was negative. There was no evidence of peripheral arteriosclerosis by roentgen examination.

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THE CLINICAL APPLICATION OF PORTAL VENOGRAPHY IN PORTAL HYPERTENSION*

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THE etiology and pathology of portal hypertension is now being intensively investigated, and relief from, or amelioration of the condition is being carried out by surgical means in several countries. If surery is to be carried out, it is essential that accurate information regarding the anatomy and function of the portal venous system can be made available to the surgeon.

A method of demonstrating the portal venous system was described by Dreyer and Budtz–Olsen[2] and is now the method of choice in several surgical centers. We used this method in 4 instances at laparotomy by injection into the spleen under visual control. All 4 patients had very high portal vein pressures—about 400 mm. of water—and all bled very profusely from the puncture wounds after withdrawal of the needle.

We therefore use the method of injection directly into a suitable mesenteric vein when the abdomen is opened. This mesenteric vein method has also been described by Leger *et al.*,[3] Moore and Bridenbaugh,[4] and Child *et al.*[1] This is carried out in patients in whom it is hoped to be able to perform a suitable shunt operation, either portocaval or splenorenal. We regard the following as contraindications to the percutaneous splenic injection method.

(1) The possibility of severe hemorrhage with the subsequent risk of emergency splenectomy in patients already in poor condition.

(2) The possibility of injection into a viscus other than the spleen.

(3) The possibility of the splenic vein being thrombosed and so preventing visualization of the portal venous system.

The method used is as follows:

(1) Preliminary intravenous urography to see that a normal left kidney is present so that a splenorenal shunt may be carried out if the portal vein is not suitable for a portocaval anastomosis.

(2) At laparotomy a suitable branch of the inferior or superior mesenteric vein is located and 30 cc. of 70 per cent diodone injected.

(3) At the end of the injection a film is exposed. This film is the upper of two films in cassettes, in a cassette tunnel under the patient, which carries a fixed grid. Two to three seconds later the second film is exposed.

(4) Exposure factors with a mobile unit are 80–85 kv., 50 ma., and one-half second. High kilovoltage screens and fast films are used.

The films are immediately processed and usually show the mesenteric vein, portal vein and its hepatic branches, and often the left gastric and gastro-epiploic veins. The splenic vein may fill by reflux, if the portal pressure is high (see Case VIII).

The second film is helpful in assessing the time of dispersal of the opaque medium, and gastric and esophageal varices are usually better shown on the latter film.

The venous pattern of the liver may be well displayed and abnormality of the pattern demonstrated in hepatic cirrhosis. The higher the portal pressure, the greater the contrast achieved as a result of stasis of the opaque medium.

This method of examination carries no risk, as all examinations are under visual control. No complications have occurred in our 70 patients so far submitted to examination by this technique.

The advantages of the method are that:

(1) The injection is under visual control.

(2) A suitable vein can be chosen—an important point, as the percutaneous method can be invalidated by a thrombosed splenic vein.

(3) A decision can be made as to whether the obstruction is intrahepatic or extrahepatic without dissection of the portal vein.

(4) It can be seen whether the portal vein is

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FIG. 1. Case I. Female, aged seven years. Spleen removed for Gaucher's disease. Normal portal venogram at time of operation. Note the slower clearing of opaque medium from right lobe of liver. Interval approximately three seconds.

suitable for portocaval anastomosis and the anatomy of the vein displayed.

The following cases serve to illustrate the use of the method and demonstrate the variation in the anatomy and pathology encountered during these examinations.

REPORT OF CASES

CASE I. G.S., female, aged seven years, was referred to this hospital from an outside hospital because of enlarged liver and spleen. The enlarged liver was thought to be probably due to a recent infective hepatitis, and she was referred back to her original hospital to convalesce. She returned a few months later with a normal sized liver, but still a large spleen. At laparotomy, portal venography was carried out, and a normal portal venous system and portal pressure was found and the spleen removed. It was found to be affected by Gaucher's disease (Fig. 1).

CASE II. S. McIl., female, aged seven years, was diagnosed as suffering from Banti's disease, and had repeated hematemeses. The portal venogram showed a grossly dilated portal vein with obstruction at its hepatic end, and with many abnormal vessels arising from it and entering the liver. This occlusion is thought to be due to involvement of the portal vein when the ductus venosus is being occluded (Fig. 2). The film also shows varicose gastric veins and some reflux into the splenic vein.

In this case the injection was made into the left gastric vein, 15 cc. of 70 per cent diodone being used. A long vein, possibly pancreaticoduodenal is seen to enter the portal vein to the right of the spine, beyond the junction of the inferior mesenteric and splenic veins, which are outlined. A splenorenal anastomosis was performed in this case.

CASE III. E.W., female, aged sixty-five. This patient had several severe hematemeses and was diagnosed as suffering from Banti's disease. Esophageal varices were seen on barium examination. The portal venogram revealed a normal portal vein with a long left hepatic branch. There is retrograde filling of the splenic vein, two branches of the inferior mesenteric vein, and marked filling of the gastric and esophageal varices. The vascular pattern of the liver is abnormal and of the type seen in cirrhosis. A portocaval anastomosis was performed (Fig. 3).

CASE IV. R.B., female, aged five years. Repeated hematemeses and a large spleen resulted in a diagnosis of Banti's disease.

In December, 1951, a splenorenal anastomosis was carried out in an attempt to preserve the portal vein for anastomosis at a later date if this should prove necessary. Unfortunately,

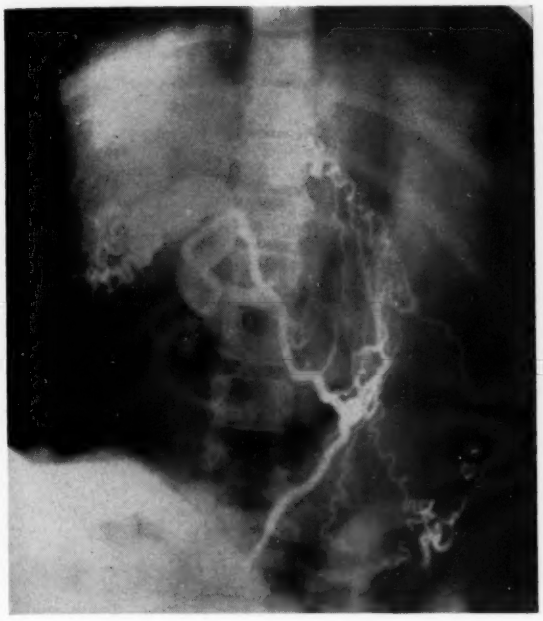

Fig. 2. Case II. Female, aged seven years. Gastro-epiploic, or pancreatico-duodenal vein entering the portal vein which is dilated and obstructed at the hepatic end, where numerous anastomotic vessels are seen to enter the liver. Numerous gastric veins filled.

further hematemesis took place and operation was again resorted to in July, 1952, when a portal venogram showed a normal portal vein as far as the porta hepatis, but numerous anastomotic vessels in this area suggesting occlusion of the vein at this point. Very gross gastric varices were also filled. A portocaval anastomosis was performed (Fig. 4).

Fig. 4. Case IV. Female, aged five years. Normal inferior mesenteric and portal veins. Great complexity of anastomotic perigastric veins, extending up to the esophagus.

Case V. T.H., male, aged three years. This

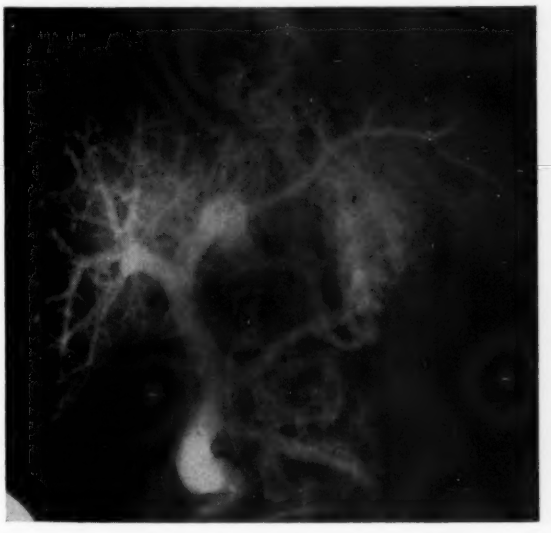

Fig. 3. Case III. Female, aged sixty-five. Normal portal vein. Filling of gastric and esophageal varices. The fine hepatic radicles have disappeared as a result of cirrhosis.

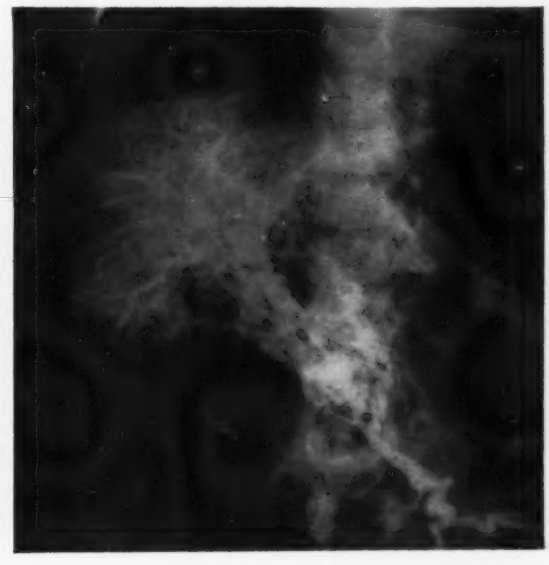

Fig. 5. Case V. Male, aged three years. Banti's syndrome. Complex system of veins replacing the portal vein, and abnormal pattern in the liver, of the type seen in cirrhosis.

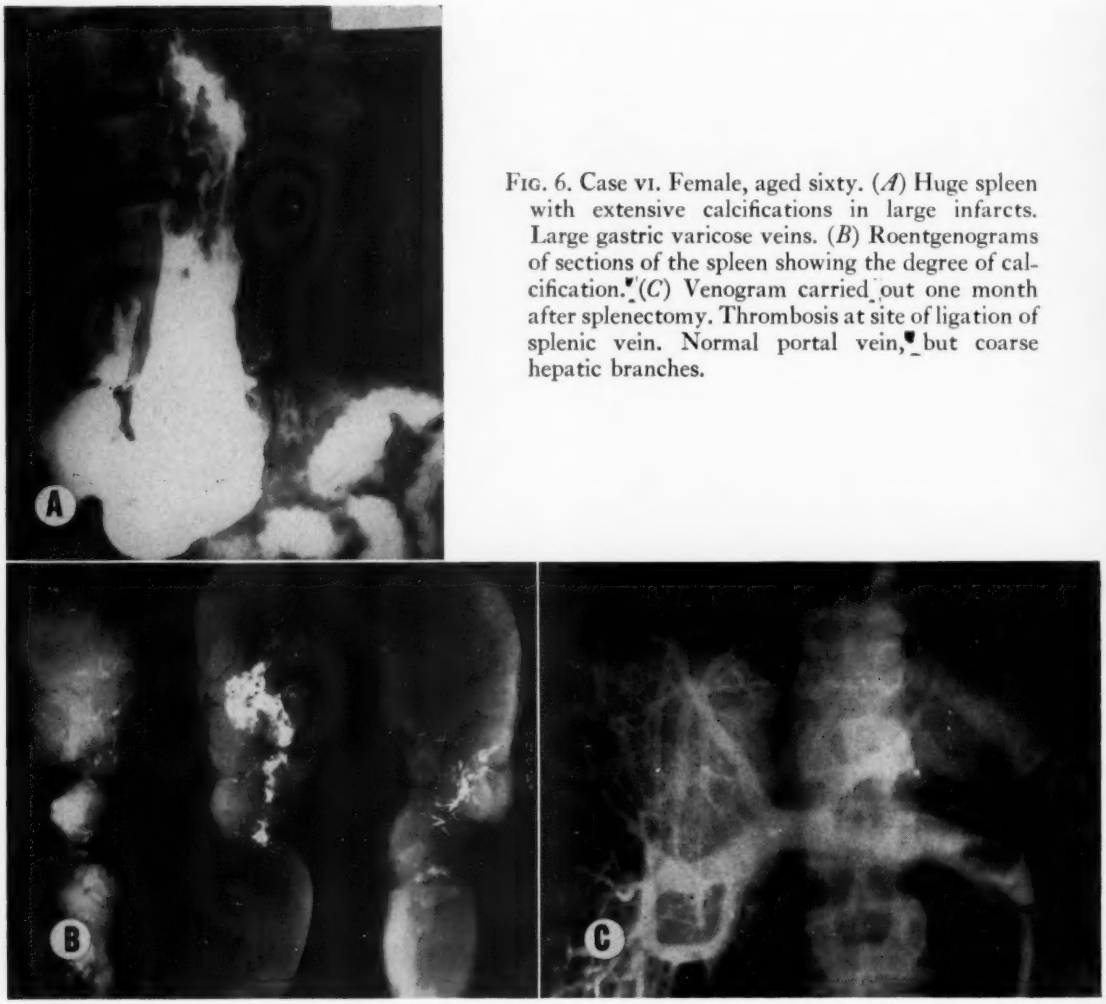

FIG. 6. Case VI. Female, aged sixty. (*A*) Huge spleen with extensive calcifications in large infarcts. Large gastric varicose veins. (*B*) Roentgenograms of sections of the spleen showing the degree of calcification. (*C*) Venogram carried out one month after splenectomy. Thrombosis at site of ligation of splenic vein. Normal portal vein, but coarse hepatic branches.

boy had attacks of hematemesis and melena, and an enlarged spleen. At operation, which was necessary owing to the persistent blood loss, the portal venogram revealed a complex system of veins replacing the normal portal vein, *i.e.*, a so-called cavernoma resulting from obliteration—developmental, or otherwise—of the portal vein. Owing to the age of the patient, a gastric trans-section was carried out to sever all the venous channels in the wall of the stomach leading to the esophageal veins from which the bleeding was taking place (Fig. 5).

CASE VI. I.M., female, aged sixty. This patient had hematemesis, anemia and an enlarged spleen. A gastrointestinal examination showed a huge spleen with large areas of calcification within it. The posterior gastric surface was much deformed and showed obvious varices. Splenectomy was carried out as a preliminary measure and was found to contain several large infarcts with calcification within them. There were also five accessory spleens producing the curious deformity of the body of the stomach. A second operation was carried out one month later and the portal venogram showed a normal portal vein with thrombosis at the site of detachment of the splenic vein. A satisfactory portocaval anastomosis was performed (Fig. 6, *A*, *B*, *C*).

CASE VII. C.C., male, aged forty-four. This man had recurrent ascites attributed to portal cirrhosis, and gross esophageal varicose veins were demonstrated by roentgen examination. A portal venogram at the time of the laparotomy showed a normal portal vein with attenuated hepatic branches, and the left gastric vein and gastric and esophageal varices were well filled. The findings were suitable for the carrying out

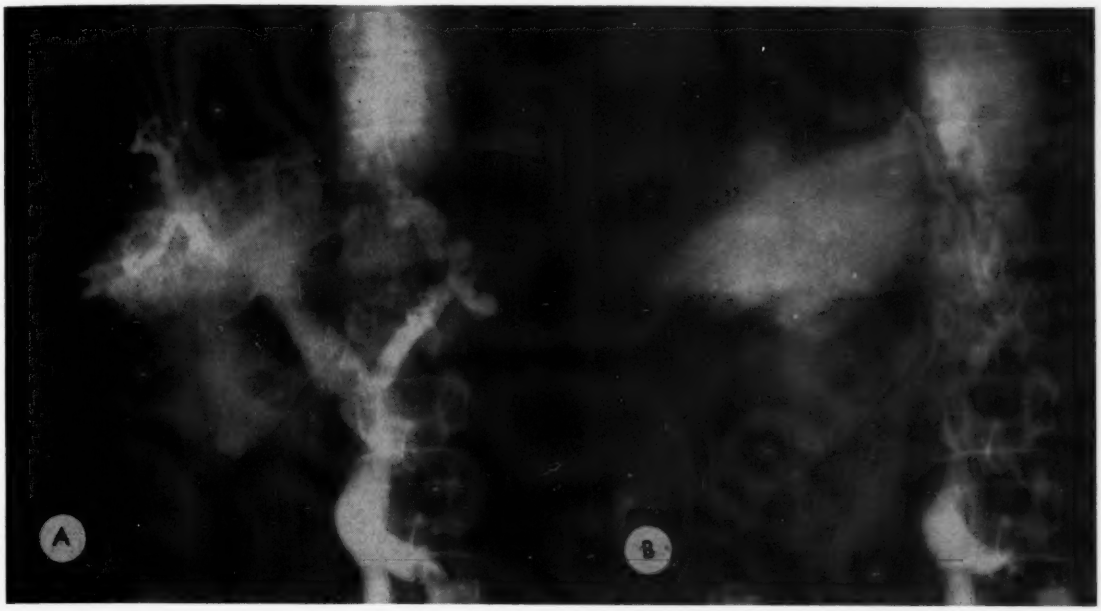

Fig. 7. Case vii. Male, aged forty-four. (*A*) Normal inferior mesenteric and portal veins, and small shrunken liver. Large left gastric vein, and varicose gastro-esophageal veins. (*B*) Delayed clearing of the opaque medium after three seconds' interval. Calcified mesenteric cyst also seen displaced to the right.

of a portocaval anastomosis and this was done (Fig. 7, *A* and *B*).

Case viii. A.C., male, aged thirty-eight. This man had ascites and was diagnosed as having portal cirrhosis. Barium examination showed esophageal and gastric varices. The portal venogram showed a dilated portal vein with numerous anastomotic channels and very sluggish circulation, as seen on comparing Figure 8*A* and 8*B* taken at an interval of three seconds. There is obviously no appreciable opacification of the liver. There is gross varicosity of the stomach and duodenum and marked reflux into the splenic vein. The portal pressure was nearly 400 mm. of water.

A portocaval anastomosis was done, but the patient's condition was such that he died a few days later. A portal venogram carried out at autopsy shows an excellent anastomotic opening between the portal vein and the vena cava (Fig. 8*C*).

It is hoped that this short report may have indicated that the method of portal venography, at the time of laparotomy, is useful, simple and free from complications. It is now regarded as an essential and integral part of the surgical attack on the condition of portal hypertension, as carried out in this hospital. This communication should be regarded as a preliminary report to be followed up by a more detailed analysis by members of the staff of this department of over 70 patients submitted to this investigation.

CONCLUSIONS

The carrying out of portal venography by injection of the opaque medium into a tributary of the portal vein at the time of the operation, affords the surgeon indispensable information regarding the state and anatomy of the portal venous system from which he is able to decide on the most satisfactory approach to the problem of relieving the portal hypertension. So far, no complications or dangers have been encountered by this method.

SUMMARY

A method of portal venography, useful in the problem of treating portal hypertension by surgical means, is described. The method has proved to be of vital importance in demonstrating the anatomy and

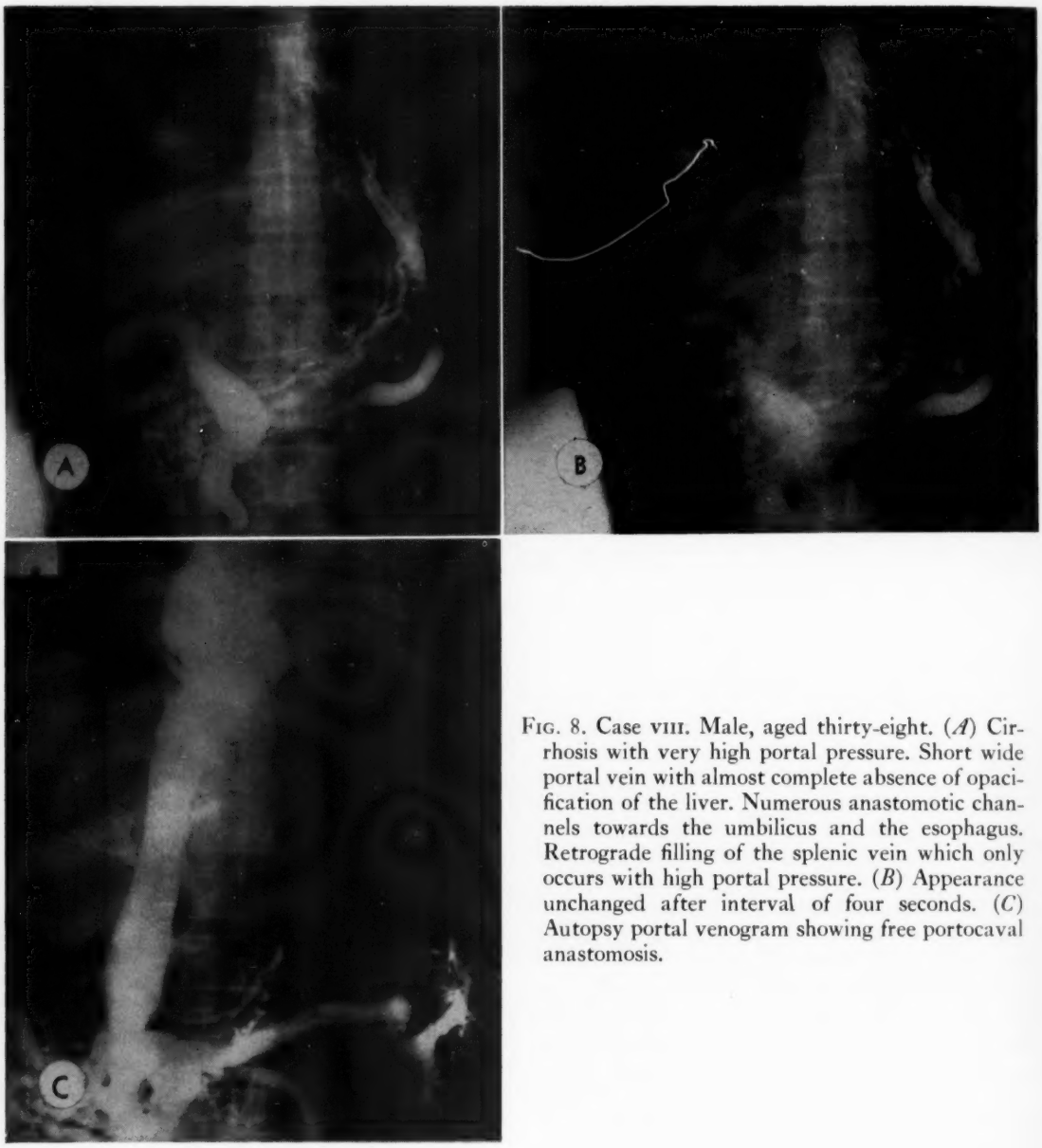

FIG. 8. Case VIII. Male, aged thirty-eight. (*A*) Cirrhosis with very high portal pressure. Short wide portal vein with almost complete absence of opacification of the liver. Numerous anastomotic channels towards the umbilicus and the esophagus. Retrograde filling of the splenic vein which only occurs with high portal pressure. (*B*) Appearance unchanged after interval of four seconds. (*C*) Autopsy portal venogram showing free portocaval anastomosis.

pathology of the portal venous system. Several illustrations are given of the different types of lesions and variations in anatomy encountered.

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It is a pleasure to pay tribute to the simulus and encouragement afforded by Mr. Alan Hunt, who has been responsible for the surgery of all patients examined, in developing a satisfactory roentgenographic technique.

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AN UNUSUAL FORM OF OSSEOUS DYSPLASIA

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IN May, 1951, an eleven year old girl was admitted to the Hospital for Crippled Children in Jerusalem. The family history was noncontributory apart from the fact that the girl's mother had been operated on for toxic goiter a few weeks before becoming pregnant. The patient is her mother's only child. The mother states that up to the age of four years the patient presented no abnormalities and talked and moved all limbs normally. During the following years the patient appeared to be weaker than other children of equal age. Two years ago the mother first noticed that the girl's back became curved. One month ago the first menstruation occurred.

On examination an unintelligent expression and marked mental retardation were noted. The girl's stance was dominated by an equinus position of the right foot and internal rotation of the right leg, by pelvic obliquity and a correctible lumbar scoliosis and by a severe fixed kyphotic deformity of the lower dorsal spine partially compensated for by exaggerated lumbar lordosis (Fig. 1 and 2). The girl finds it difficult to keep her balance and can therefore not stand still.

The right hip is kept in internal rotation and can be rotated externally to neutral position only. Extension and adduction to normal range, but flexion and abduction are restricted. There is valgus position of right knee. The motility of the left hip and knee is practically normal. Both feet show deformities and shortening of all toes, two toes on each foot only possess a nail. The child can by active movement overcome the equinus position of the right foot when strongly admonished to do so. When she does, her legs are of equal length, the pelvic obliquity disappears and the scoliosis is corrected.

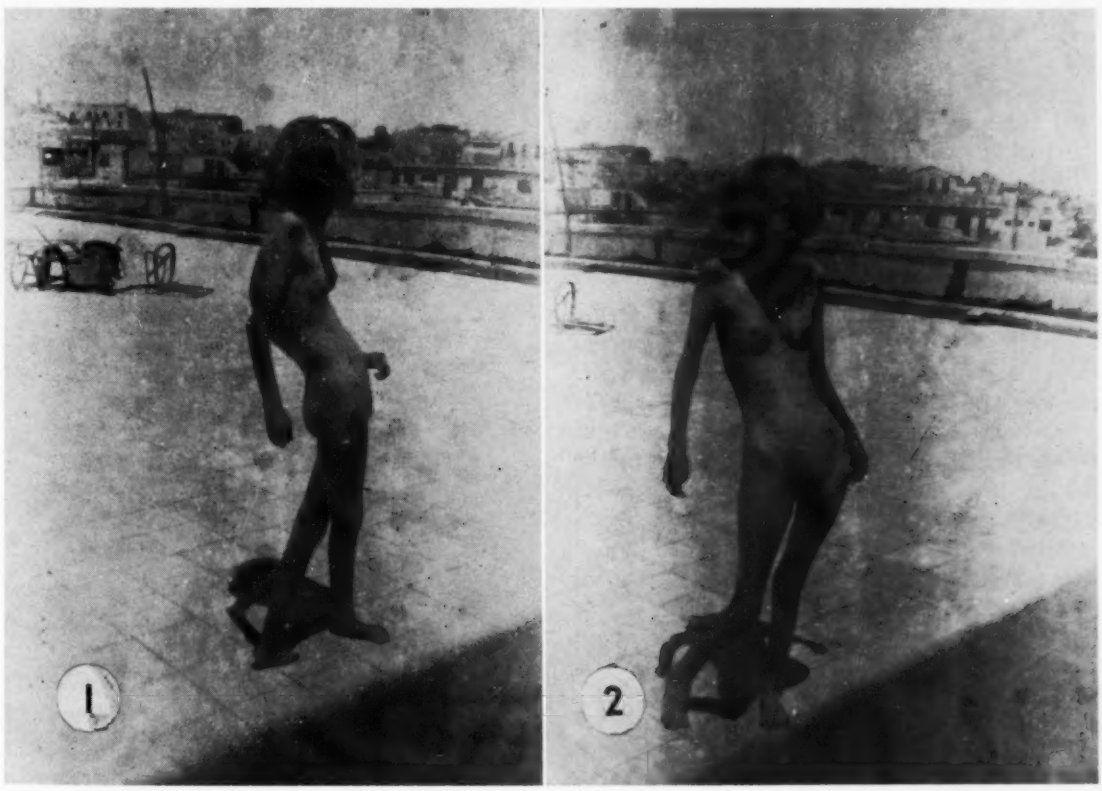

FIG. 1 and 2. Eleven year old girl. Sexual precocity. Lumbodorsal kyphosis and exaggerated lumbar lordosis. Pelvic obliquity and static scoliosis. Right leg in internal rotation, right knee in valgus and right foot in equinus position. Instability of stance.

FIG. 3. Lateral roentgenogram of spine taken in June, 1951. Cephalocaudally long and ventrodorsally short lumbar vertebrae. Partial fusion (undersegmentation) of 10th, 11th and 12th dorsal vertebrae, which form apex of kyphotic curve. Partial fusion of 8th and 9th dorsal vertebrae. Radiopaque shadows in lumbar intervertebral spaces.

Both upper extremities present a normal range of movement in all joints, but muscles of both shoulders and arms are visibly underdeveloped. The right index and both fifth fingers possess only two phalanges. Some fingernails are absent, some are deformed. Those nails present are short and thin.

Apart from a generally bad condition of the child's teeth and from a high arched palate no further abnormality was detected by physical examination. The girl was of normal height corresponding to her age and in fair nutritional state. The corneas were clear and vision was good. The girl complained occasionally of pain in her ears, but the ears were repeatedly reported to be normal by the consulting specialist. There was strong menstruation lasting for seven days. Liver and spleen not enlarged. Blood pressure 85/55.

Laboratory Findings. Normal sedimentation rate. Blood count normal apart from a moderate degree of hypochromatic anemia. Glucose, calcium, and phosphorus levels in the blood normal. Kahn and Wassermann reactions negative.

Roentgen Findings. Skull: Abnormally small mandible. Otherwise nothing abnormal, pituitary fossa not enlarged.

Spine (Fig. 3): The bodies of the lumbar vertebrae are notable for their height as compared with their short transverse diameter and thereby recall a dog's vertebrae. There are calcifications in the lumbar intervertebral spaces. The bodies of the tenth, eleventh and twelfth dorsal vertebrae are fused in their anterior parts and form the apex of the kyphotic curve. The upper plate of the tenth and the lower plate of the twelfth are irregularly shaped in their anterior parts. The bodies of the eighth and ninth dorsal vertebrae also appear to be partially fused.

Hands (Fig. 4): The bones are long and slender. In the fingers, whose distal phalanges

FIG. 4. Hands and feet of eleven year old girl. Bone age assessed from this film as fourteen years. General osteoporosis. Finest trabeculation (ground glass appearance) best seen in diaphyses of first metatarsals. In several fingers and toes one or two phalanges are missing; in those fingers and toes the most distal bone is deformed.

are missing, the middle phalanges are tapered into a short pointed end. The bone age has been assessed as fourteen years (chronological age eleven years) judged by the following maturity indicators: considerable "capping" of the radial epiphysis which has not yet fused with its shaft. The ulnar epiphysis follows closely the contour of the shaft. Capitate, hamate, triquetral and navicular have attained their adult shape. The epiphyses of the first metacarpal and of all phalanges except the third proximal have fused with their shafts. The epiphyses of the 2nd, 3rd, 4th and 5th metacarpals are in the process of fusing with their shafts.

Feet (Fig. 4): Metatarsals are long and thin. In all but the left big toe one or two phalanges are absent and in all toes the most distal bone is deformed tapering out into a pointed end. All epiphyses have completely or nearly completely fused with their shafts. There is slight general osteoporosis; the metatarsal diaphyses show the finest trabeculation (ground glass appearance).

A complete skeletal survey could not be carried out as unfortunately we have to economize on films. One tibia and the bones of one forearm also show the finest trabeculation.

Treatment consisted in a moderately successful attempt to encourage the formation of compensatory lordotic curves near the kyphotic apex by the customary means and in re-educational efforts to improve stance and gait. The fact that the girl when strongly admonished was able to bring her right foot up into neutral position and to stand properly and her poor mental condition and lack of cooperation in physiotherapy precluded surgical means of improving stance and gait.

Fig. 5. Lateral roentgenogram of spine taken August, 1950. Radiopaque shadows are seen in the intervertebral spaces of the lower dorsal spine which are not visible in the later film (Fig. 3). Lumbar spine shows early beginning of calcification in intervertebral spaces as compared with later film (Fig. 3).

DISCUSSION

The interpretation of the findings and the classification of the case presented difficulties. Cephalocaudally long and ventrodorsally short vertebral bodies have been observed by Caffey in a case of gargoylism. Dull facial expression, mental retardation, defective teeth, limitation of motion in one or more joints and dorsolumbar kyphosis are considered constant signs of this condition. Our case recalls that in 1 of the 2 cases of gargoylism reported by Caffey the child's mother suffered from goiter during pregnancy. But while in gargoylism the dorsolumbar kyphosis is the result of anterior wedging of a vertebral body at this junction (Luck and others), the deformity in the case discussed here is due to partial fusion of several vertebral bodies, probably a congenital anomaly (undersegmentation, Caffey) which, however, is rare at that particular level.

The roentgenological appearance of the tubular bones, including the long and slender metacarpals, do not seem to fit in with this diagnosis, nor does the lack of clouding of the corneas. But this might still be a forme fruste of gargoylism (Jervis) as any one of the classical symptoms of the condition may be absent and deformities of the bone may be of such mild degree as to escape attention. Straus *et al.* have also recently reported a case which showed no abnormalities of bones and joints except

for slight osteoporosis of disuse. The fact that in our case the distal end of the second (here terminal) phalanx of the right index finger and of most toes tapers to a narrow point and appears to be "pinched off," fits in with Caffey's description.

Sexual precocity and early epiphyseal union as seen in the present case, however, seem to rule out a diagnosis of gargoylism, in which condition, on the contrary, delayed fusion has frequently been described; these signs point to an endocrine disturbance, probably of the pineal gland, although nonendocrine acceleration of osseous development has been described (Wagner and others).

The radiopaque shadows between the bodies of the lumbar vertebrae were originally interpreted as calcifications within the intervertebral discs; but when we had an opportunity to study another film taken of this girl's spine ten months earlier in another hospital (Fig. 5), we found similar shadows in the intervertebral spaces at different levels, particularly in the lower thoracic spine which presented no such findings in the later film. This fact, viewed in the light of the recent publication by Bick and Copel, makes it more likely that the radiopaque shadows correspond to an extraordinarily strong calcification of the apophyseal ring of the vertebral body. This also makes it probable that here an endocrine dysfunction is being dealt with and together with the high arched palate (Moehlig) directs the thought to the pituitary gland.

Absent or dysplastic fingernails are occasionally seen in cases presenting congenital osseous anomalies (Mino, Thompson) and cannot be considered unusual. Nor are the normal blood calcium and phosphorus readings of differential diagnostic value, as this is usually found in genetic and occasionally in endocrine anomalies.

In conclusion, it may be said that some of the symptoms presented by this case, especially the high and narrow vertebral bodies and the restriction of movements in several joints recall the picture of a forme fruste of gargoylism, while sexual precocity, early epiphyseal fusion and the abnormally strong calcification of the apophyseal ring of the vertebral bodies caused us to abandon this diagnosis and to assume that this is a case of glandular dysfunction in which pituitary and pineal glands are involved.

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I have pleasure in thanking Dr. E. Heilbronner, Director of the Hospital for Crippled Children in Jerusalem, for permission to report the case.

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ROKITANSKY-ASCHOFF SINUSES OF THE GALLBLADDER DEMONSTRATED ROENTGENOGRAPHICALLY*

REPORT OF A CASE

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A SEARCH of the literature disclosed only 2 cases of Rokitansky-Aschoff sinuses of the gallbladder visualized by roentgenography. The first case was that of March[1] in 1948 and the second by Bean and Culver[2] in 1950. Both of these gallbladders had sinuses in conjunction with other deformities of the organ.

The gallbladder has neither a submucosa nor a muscularis mucosae so that the mucosa is in immediate contact with the muscular layer. Occasionally, small diverticula extend from the mucosa, through the muscularis into the serosa. Many of these cases are associated with chronic inflammation and the presence of stones. These structures are known as Rokitansky-Aschoff sinuses but, according to Foot,[3] they were first accurately described by Morgagni in "De sedibus, et causis Morborum per anatomen indagatis" and they should therefore bear his name rather than that of Rokitansky. Aschoff was the first modern pathologist to give them much attention.

Rokitansky-Aschoff sinuses are outpouchings of the mucosa through the muscularis of the gallbladder wall. It is thought that they represent herniations of the mucosa through interstices between the muscle bundles of the gallbladder wall.

Rokitansky in 1842 called attention to hernia-like out-pouchings of the gallbladder mucosa toward the external layers of the gallbladder. Aschoff in 1905 called them "Luschka ducts," emphasizing their pathological significance in connection with biliary stasis of the gallbladder and the formation of gallstones. It was later pointed out that these structures were not the aberrant bile ducts in the wall of the gallbladder discovered by Luschka in 1863. In nondiseased gallbladders, these sinuses are rarely seen and if present they are quite shallow. Gallbladders that have well formed sinuses are usually thickened, fibrous, and chronically inflamed. Apparently in these organs, the contractile elements are weakened and the intermuscular septa are widened by overdistention, thereby producing these herniations.

CASE REPORT

The patient, H.P., female, white, aged thirty-six, entered the hospital on November 26, 1950 complaining of epigastric pain of several months' duration. This pain usually started at night, two hours after supper and continued until morning or until she took food. Milk usually relieved her symptoms. Again the pain recurred one or two hours after breakfast and just before supper. There was no associated melena or hematemesis. Nausea and vomiting were absent and bowel movements were considered normal. She had had similar symptoms four years previously, at which time a diagnosis of gastric ulcer was made. This was treated medically with marked relief but her symptoms returned several months before this admission. Her family and personal history were noncontributory. Her previous health other than the ulcer was good.

Physical examination disclosed an apparently healthy thirty-six year old white female in no acute distress. The eyes, nose and throat were normal. The heart was within its normal border, had normal sounds and no murmurs. Both the rate and rhythm were normal and the blood pressure was 110/64. The temperature was normal.

The abdomen disclosed tenderness in the

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FIG. 1. The gallbladder concentrated the priodax quite well outlining the "double gallbladder."

epigastrium but no masses were palpated. The external genitalia and the extremities were normal.

Laboratory findings indicated normal urinalysis, red blood cell count of 3,800,000 with 11.5 grams of hemoglobin and a white blood cell count of 10,450, with 67 per cent polymorphonuclears and 33 per cent lymphocytes.

Roentgen Findings. Oral cholecystography revealed a gallbladder of average density presenting a constriction just below the neck. This gave the appearance of a double gallbladder and was persistent throughout the examination (Fig. 1). Neither pouch contained calculi. Surrounding the lower segment only, best seen on the routine films, was a stippled, halo-like extravasation of the contrast medium beyond the normal lumen of the gallbladder (Fig. 2). This we recognized as typical of the escape of the medium into the patent Rokitansky-Aschoff sinuses. The one hour follow-up post-fatty meal films showed the upper pouch to be completely empty of the contrast medium with sluggish contractility of the lower pouch. The sinus filling was again seen. The entire series of films was repeated four days later with duplication of the original findings. A study of the gastrointestinal tract revealed a chronic duodenal ulcer, nonobstructive and without signs of any activity.

Operation. A cholecystectomy was performed with the removal of a thick-walled gallbladder.

Pathology. Gross (Fig. 3): The specimen consists of a gallbladder 8 cm. in length by 2.5 cm. in diameter. The serosa is generally soft, slightly roughened and grayish while the wall is thickened to 0.5 cm. and, under finger pressure, small nodules can be felt distributed rather evenly throughout. Upon sectioning the organ, small cysts in equal distribution are noted in the wall, becoming less visible at the pouches. They are from pinpoint to 0.2 cm. in size, contain black friable concretions and are surrounded by distinct zones of grayish firm tissue. These communicate with minute openings in the mucosa which are quite visible upon stretching the wall and are equally distributed. The mucosa is green and velvety and is divided into three compartments: one main central com-

FIG. 2. A halo-like stippling surrounds the gallbladder shadow as the material fills the Rokitansky-Aschoff sinuses.

Fig. 3. Opened specimen shows the three separate pouches. Note black concretions filling the Rokitansky-Aschoff sinuses which had free communication with the gallbladder lumen.

partment and two small pouches, one at the fundus which is 2 cm. and the other at the distal portion which is more narrow and 1.5 cm. in length. It would seem from the cut section at this point that the bile duct is dilated. Though the roentgen examination revealed one constriction, the removed specimen disclosed two as described above.

Microscopic: Sections of the gallbladder disclose generalized thickening produced by hypertrophy of the muscular layers and an increase in the fibrous tissue separating muscle bands and in the serosa. The mucosa is ulcerated and the villi present are blunted, thick and not evenly distributed and there is a moderate lymphocytic infiltration. The characteristic feature is the presence of Rokitansky-Aschoff sinuses situated mainly in the serosa. They are slightly irregular, large and are lined by a tall columnar epithelium. Brownish concretions are noted within many of the lumens. The sinuses are surrounded generally by thick zones of fibrous tissue heavily infiltrated with lymphocytes. In a number of sections, sinuses are seen arising from the mucosa separating bands of muscle tissue and extending outward into the serosa.

DISCUSSION

The rarity of this condition roentgenographically deserves reporting even though occasionally one notes a case in the pathological laboratory not visualized on the roentgenogram. Our case manifested findings very similar to the 2 reported in the literature except that sinuses were present in all sections of the wall in contrast to the 2 reported cases where sinuses were localized to that part of the wall distal to the constriction. All 3 cases had constrictions except that our case had two, one at the neck and the other at the fundus and it would appear that they were congenital in type.

SUMMARY

1. A case has been presented of Rokitansky-Aschoff sinuses of the gallbladder demonstrated by oral cholecystography.

2. The condition is discussed anatomically and roentgenologically, with reference being made to the literature.

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HYPAQUE, A NEW UROGRAPHIC CONTRAST MEDIUM*

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NEW urographic constrast media constantly are being sought and tried with a view to improving the diagnostic quality of the urograms and to reducing the incidence of postinjection reactions in patients. A new contrast medium, Hypaque,† was administered to a series of 350 patients with encouraging results.

Hypaque is a white crystalline solid (sodium 3, 5 diacetamido-2, 4, 6-triiodobenzoate) with a molecular weight of 636.0. It is supplied in the form of 30 cc. ampules that contain a 50 per cent solution of the sodium salt. Hypaque contains 59.8 per cent iodine by weight, as compared with the other urographic contrast media: urokon sodium, which contains 65.8 per cent; diodrast, which contains 48.9 per cent; and neo-iopax, which contains 51.5 per cent.

McChesney[1] demonstrated in dogs that Hypaque is excreted almost entirely through the kidney in an unchanged form following intravenous administration. Most of the contrast medium was excreted within two hours. Additional experiments[1] have shown that Hypaque is well tolerated by mice, rats, rabbits, and monkeys. In a preliminary study[1] of a series of 150 patients in whom Hypaque was utilized as the constrast medium for urography, visualization of the kidneys was consistently satisfactory. Minor reactions were observed in only 3 of these patients; 1 complained of slight dizziness, 2 of flushing. No other side effects were noted.

PROCEDURE

This series of 350 patients consisted of 187 men and 163 women ranging in age from seventeen to seventy-nine years and ranging in weight from 97 to 280 pounds. All were ambulatory, but no attempt at other selection was made. For each patient a "urogram survey sheet" was used on which were indicated the patient's clinic number, age, race, weight, and sex. A brief allergic history was recorded on the sheet by having the nurse list any allergy prior to the injection of the contrast medium.

Each patient received 25 cc. of Hypaque intravenously, usually in the antecubital vein, and the length of time taken for the injection was recorded. This varied from one to three minutes. The postinjection reactions, if any, and the diagnostic rating of the urograms were later recorded on the same survey sheet. The urogram series for each patient consisted of five films; two with compression which were made five and fifteen minutes after injection; two without compression made sixteen and thirty minutes after injection; and one film of the bladder.

REACTIONS

Twenty of the patients gave a history of previous allergies: 9 had histories of hay fever, 6 of asthma, 3 of food allergy, 1 of hives, 3 of dust allergy, and 1 of allergy to cat and dog dander. Following the injection of Hypaque, only 34 (9.7 per cent) of the 350 patients experienced one or more reactions (Table 1). Interestingly, the incidence of reactions to Hypaque was nearly three times higher in the 20 patients with histories of allergies than it was in the remainder of this series (25 per cent as compared with 8.9 per cent).

The percentage of patients having reactions in this series (9.7 per cent) is significantly less than that which has been re-

† The Hypaque was generously furnished by W. A. Curran of Winthrop-Stearns, Inc., 1450 Broadway, New York 18, New York.

* From the Department of Roentgenology, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute, Cleveland, Ohio.

Table I

POSTINJECTION REACTIONS IN 34 PATIENTS

Reaction	Incidence
Nausea	12
Bad taste	10
Vomiting	8
Dizziness	4
Warmth	4
Flushing	3
Hives	3
Moderate pain at site of injection	2
Coughing	1
Fainting	1
Pallor	1
Sweating	1

ported from the Cleveland Clinic when other contrast medium has been employed: *e.g.*, 14.7 per cent of 1,000 patients who received diodrast had one or more reactions;[2] 18.6 per cent of 1,000 who received neoiopax had one or more reactions;[2] and about 45 per cent of 1,000 who received urokon had one or more reactions.[3]

On the advice of the manufacturer, a longer injection time, *e.g.*, three minutes, was used for the first group of patients. The next group was injected over a two-minute interval, and finally the injection time was reduced to one minute. From Table II it is apparent that slow injection is not necessary and may even promote a reaction. In a few of the patients the contrast medium was infiltrated into the subcutaneous tissue about the site of injection. None of these complained of any great degree of burning or discomfort in the area of infiltration.

DIAGNOSTIC RATINGS OF UROGRAMS

The urograms were rated on the basis of diagnostic quality and scored on the survey sheets according to the criteria devised by Hoppe[1] (Table III). In many of the cases of this series, visualization was particularly excellent on the five-minute film. In general, the "pyelogram-like" contrast was striking. The one urogram that showed no visualization was repeated the following day and the urinary tract was then visualized satisfactorily. Of the 11 patients with visualization on one side only, 6 had had nephrectomies, and 1 had a large stag-horn calculus on the side that showed no evidence of renal function.

Table II

Duration of Injection	No. of Patients	No. of Reactions	Per Cent of Reactions
1 minute	245	20	8.2
2 minutes	66	7	10.6
3 minutes	39	7	17.9
Total	350	34	9.7

In several cases, urograms that previously had been obtained in these patients with other contrast media, were compared with those of this series; in every one of these instances visualization with Hypaque was better than it had been in the previous examination.

Table III

DIAGNOSTIC RATINGS OF UROGRAMS*

A. Morphology of upper urinary tract	
No visualization	1
Upper third of either or both ureters faintly visible	3
Upper third of either or both ureters distinctly visible	4
Calyces, pelvis and upper ureter of one side visible	11
Calyces, pelvis and upper ureter distinctly visible on one side with partial visualization on other side	53
Calyces, pelves and upper ureters of both sides distinctly visible	278
B. Only the bladder visible	0
C. Roentgenographic quality (density of shadows)	
No visualization	1
Poor—shadows barely visible, morphology indistinct	8
Fair—faint but distinct outlines	24
Good—distinct shadows of unquestionable diagnostic quality	165
Excellent—brilliant shadows, structures stand out in bold relief in contrast to surrounding tissues	152

* Criteria according to Hoppe.[1]

SUMMARY

The value of Hypaque as a urographic contrast medium is twofold: it makes possible excellent visualization of the urinary tract, and it diminishes the number of post-injection reactions.

In a series of 350 patients, less than 10 per cent had any type of reaction following injection of the medium, and in general the urograms obtained were "pyelogram-like" in quality.

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Vol. 73, No. 5

CLINICAL EVALUATION OF A NEW COMPOUND FOR INTRAVENOUS UROGRAPHY*

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SODIUM diatrizoate, Hypaque, is a new experimental intravenous urographic compound.† The material is supplied as a 50 per cent solution in 30 milliliter ampules. It is described as a white crystalline solid containing 59.87 per cent iodine, highly water soluble, and with a molecular weight of 636.

Data[1] supplied on animal studies, in which the experimental material was compared to iodopyracet, diodrast, and sodium acetrizoate, urokon, indicated a low order of toxicity for the compound. Three minor reactions were reported in the only series of 150 patients.

Metabolic studies[1] in dogs showed that the experimental compound arrived unchanged, with 97 per cent found in the urine and 2.5 per cent in the feces, in three days. Approximately 66.5 per cent is excreted in two hours and over 90 per cent in twenty-four hours.

It was decided to compare this new material with sodium iodomethamate, neoiopax, on a clinical basis. Sodium iodomethamate is a polyiodo compound containing 51.5 per cent of the halogen and is supplied in 30 ml. ampules as a 50 per cent solution. In the five year period in which this material has been utilized at University Hospitals of Cleveland for intravenous urograms, no death or serious reaction has occurred in more than 15,000 examinations.

METHOD

Case report forms, in which all essential data could be recorded, were filled out for each patient. Every other patient received an ampule of sodium iodomethamate and the others an ampule of sodium diatrizoate. Vital signs were recorded before injection, after the five minute film, and between the ten and the fifteen minute films. Each patient was observed and questioned for untoward signs and symptoms as recorded in Table 1. Thus no deviation from the routine procedure was undertaken other than the recording of certain data.

After 200 consecutive cases, 100 with either compound, the films were assembled by cases in random piles for evaluation of diagnostic quality. The criteria used were as follows:

Superior—diagnostic quality equal to an excellent retrograde pyelogram.

Satisfactory—of sufficient definition, contrast and density to rule in or rule out any abnormality.

Unsatisfactory—subdiagnostic definition, contrast and density.

The calyces and pelves were the only anatomic structures evaluated, as visualization of the ureters and bladder in their entirety is not a necessary function of intravenous urography.

Not knowing which compound had been injected in a given patient, and independent of each other, the three evaluating radiologists designated one of the possible three categories for each case after reviewing the films.

The final category for each case was then decided by majority opinion and tabulated as shown in Table II.

RESULTS

Examination of Table 1 shows no significant difference as concerns patient response to either urographic material. No reactions of a serious nature occurred with either compound. A description of general warmth and a metallic taste in the mouth

† Material supplied by Winthrop Stearns, Inc.

* From the Department of Radiology, University Hospitals of Cleveland, Cleveland, Ohio.

TABLE I

NUMBER OR PER CENT OF 100 PATIENTS DEVELOPING UNTOWARD SIGNS AND SYMPTOMS AFTER THE INTRAVENOUS ADMINISTRATION OF SODIUM DIATRIZOATE AND SODIUM IODOMETHAMATE

Signs and Symptoms	Sodium Diatrizoate	Sodium Iodomethamate
I. Objective data		
A. Vital signs		
1. Temperature (oral)	0	1
2. Pulse	0	1
3. Respiration	0	3
4. Blood pressure	0	1
B. Gastrointestinal		
1. Emesis	2	2
C. Cardiorespiratory		
1. Shortness of breath	0	0
2. Wheezing	0	0
3. Cyanosis	0	0
4. Pallor	0	0
D. Autonomic		
1. Sweating	1	0
2. Salivation	2	1
3. Flushing of skin	3	1
4. Fainting	0	0
5. Urticaria	0	0
E. Cough and/or sneezing	2	0
II. Subjective data		
A. Autonomic		
1. Itching	0	0
2. Dizziness	2	0
3. Pain in injection arm (vein cramp)	0	3
4. General warmth	100	100
5. Taste in mouth	100	100
B. Gastrointestinal		
1. Nausea	12	11
C. Cardiorespiratory		
1. Constriction of chest	0	0
2. Choking sensations	0	0

NOTE: Excluding the categories of warmth and taste, a total of 18 patients developed one or more reactions to sodium diatrizoate and a total of 15 patients developed one or more reactions to sodium iodomethamate.

could be elicited from all the patients in each group and a little more than 10 per cent of the patients complained of nausea.

TABLE II

NUMBER OR PER CENT OF 100 PATIENTS FALLING INTO DEFINED CATEGORIES OF GRADING INTRAVENOUS SODIUM DIATRIZOATE AND SODIUM IODOMETHAMATE UROGRAMS

Compound	Unsatisfactory	Satisfactory	Superior
Sodium diatrizoate	15	46	39
Sodium iodomethamate	38	55	7

Table II shows that of 100 cases receiving intravenous sodium diatrizoate, 39 resulted in superior film studies, 46 were satisfactory, and 15 were unsatisfactory. In contrast, 7 superior, 55 satisfactory, and 38 unsatisfactory film studies resulted from the intravenous administration of sodium iodomethamate in 100 cases.

The striking difference of 39 superior film studies produced with sodium diatrizoate and 7 produced with sodium iodomethamate was found to be statistically significant. Also confirmed by statistical methods is the difference between 15 unsatisfactory film studies produced with sodium diatrizoate and 38 with sodium iodomethamate. When the few obviously poorly prepared cases are excluded from the study, the differences between the two contrast materials for the categories of superior and unsatisfactory film studies hold essentially the same statistical significance. This seems to indicate that the greater radiopacity of sodium diatrizoate makes its use less dependent upon preparation of the patient or renal function.

No statistically significant difference exists between the two compounds for the category of satisfactory film studies.

The members of the evaluating group were impressed by the brilliance and sharp definition rendered by sodium diatrizoate. During the evaluating procedure, two of the panel recorded guesses as to which material had been used in each case. Analysis of these data showed remarkable statistical correlation. Seventy per cent of

the time each could distinguish between sodium diatrizoate and sodium iodomethamate.

It was interesting to note that 15 of the sodium diatrizoate cases and 11 of the sodium iodomethamate cases had allergic histories. This fits well with the fact that 10 to 15 per cent of any large random population will have allergic histories. In our study the histories ranged from iodism, asthma and antibiotic allergies to the pollen and food allergies. Four out of the 15 sodium diatrizoate cases and 2 out of the 11 sodium iodomethamate cases manifested reactions. There was no statistical difference between these two groups nor any difference between the allergic and nonallergic groups as to incidence or type of reaction. Furthermore, there was no relationship between type of allergy and type of reaction.

After the 200 cases discussed in the prior paragraphs were evaluated, the next 178 patients requiring intravenous urography were injected with sodium diatrizoate. These 178 cases were treated as routine cases. There was no difference in reactions between this group and the first 200 cases.

SUMMARY

One hundred out of 283 cases of a new polyiodo intravenous urographic compound, sodium diatrizoate (Hypaque), were compared statistically and clinically with 100 cases of sodium iodomethamate.

Sodium diatrizoate reveals a remarkable incidence of superior studies and a significantly low incidence of unsatisfactory visualization when compared to sodium iodomethamate.

Patient reactions to sodium diatrizoate are no different in incidence or type to sodium iodomethamate which is considered a remarkably safe intravenous iodine compound by this department.

Excretion rate of sodium diatrizoate appears to be clinically similar to that of sodium iodomethamate. Thus, the usual examination can be completed in the total time of approximately twenty minutes.

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We wish to acknowledge the help in carrying out this study of George Franklin Badger, B.S., M.P.H., M.D., Professor of Biostatistics, School of Medicine, Western Reserve University, and Walter Neubrander, Chief Technician, Department of Radiology, University Hospitals of Cleveland.

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A METHOD FOR MEASURING THE RATE OF ELIMINATION OF RADON IN BREATH

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I. INTRODUCTION

FOR the study of the toxicity of radium now being carried on at Argonne National Laboratory, it is necessary to make accurate measurements of the amount of radium retained in the bodies of living humans several years after radium intake. In the portion of this work reported here, a procedure is described which permits measuring the radon content of exhaled breath to much greater sensitivity and with better accuracy than previously reported for such analyses.

Since radium disintegrates with the emission of alpha rays which do not have sufficient penetrating power to be detected externally, its quantification in living humans is based primarily on the properties of its radioactive descendants. One microgram of Ra^{226} forms 2.1×10^{-12} curies of Rn^{222} per second. Some of the radon, a rare gas, escapes from the site of formation and is eliminated in exhaled breath, while the remainder disintegrates in the body and deposits other radioactive nuclides, some of which emit highly penetrating gamma rays. At radioactive and physiological equilibrium, the amount of radium in the body, X micrograms, may be expressed in terms of radon as

$$X = B + \frac{E}{2.1t} \qquad (1)$$

where B is the number of microcuries of radon which disintegrate in the body and E is the amount of radon, expressed in units of micromicrocuries ($\mu\mu$c.), which leave the body in t seconds. Thus, the total amount of radium is obtained as the sum of two measurements: one portion of the radium is determined by measuring the rate of gamma-ray emission from the radioactive decay products in the body, and the other portion is determined by measuring the time rate of elimination of radon in the breath. This paper is concerned with the latter analysis, and the procedure for the analysis by gamma-ray measurements is described elsewhere by Marinelli, Miller and Gustafson.[16]

Evans[6] found that an average of about 45 per cent of the radon from radium remaining in the body several years after intake is exhaled in the breath. Assuming that the normal breathing rate is about 5 liters per minute, he then calculated that 1 micromicrocurie of radon per liter of breath indicates a total of about 0.1 microgram of radium "fixed" in the body. Since the maximum permissible level for "fixed" radium is 0.1 microgram[18] and as little as 0.1 micromicrocurie of radon can be measured[1,4] it has been common practice to sample only 1 or 2 liters of breath for purposes of health monitoring or for studying cases of radium poisoning.[7,9]

Although this technique has been found convenient in surveys of industrial installations, it was thought advisable in our case to obtain a more representative sample of the radon exhalation rate by lengthening considerably the collection time and by using apparatus which permits the subject to breathe more naturally during the sampling period. It would then be possible (a) to assay precisely the volume of breath exhaled per unit time, which may vary with the individual,[2] (b) to increase the accuracy of measurements on subjects having small radium burdens, and (c) to minimize the effect of transient fluctuations in the radon concentration of the breath.[10]

The analytical procedure described in

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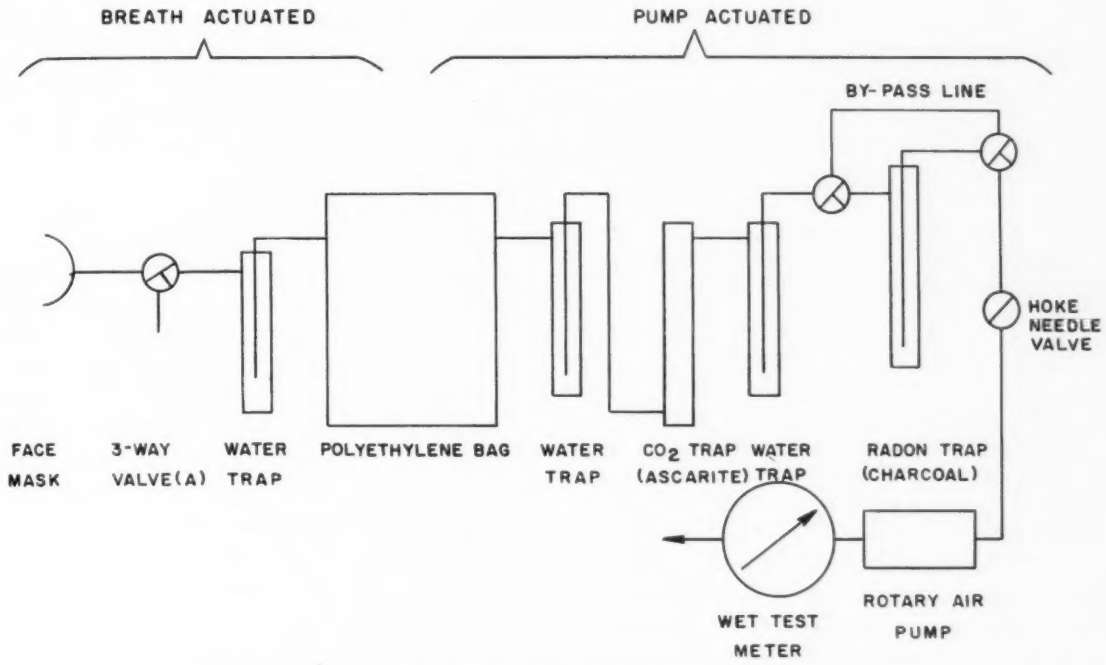

Fig. 1. Diagram of apparatus for collection of breath radon on charcoal.

this report utilizes adsorption on charcoal as a means of concentrating radon from breath. Although retention of radon by charcoal was investigated soon after the discovery of radon,[3,22,23] its application to breath analyses has received little attention. Neitzel[19] and Nikitin and Joffe[20] considered charcoal as a means of protection from inhalation of radon, Hollcroft and Lorenz[11] collected exhaled radon from mice on charcoal, and Hursh[12] recently reported on the use of charcoal for collection of field samples. The chief objection to the use of charcoal for long sampling periods probably has been the exertion of the subject in breathing through a trap filled with charcoal granules. The sampling apparatus developed in the present work avoids this difficulty; moreover radon-free air can be supplied and continuous breath samples taken for as long as the subject is willing to sit or lie quietly.

For measurement, the collected radon is desorbed into an ionization chamber connected to an electrometer or into a proportional counter. Procedures and calibrations for both of these instruments are described.

II. COLLECTION OF RADON

Figure 1 is a diagram of the collection apparatus which was developed in order to sample breath for extended periods. The subject breathes into a mask or basal metabolic rate mouthpiece fitted with valves which allow air to be inhaled from the room (or a tank of aged air) but exhaled only into the apparatus. The flexible polyethylene bag of about 20 liter capacity acts as a reservoir which prevents significant changes in the pressure of the atmosphere into which the subject exhales. The subject breathes into the bag for about one minute before the needle valve is opened, thus causing the accumulation of about 7 liters of breath; then the valve is opened wide enough to permit a vacuum pump operating continuously to draw air through the line at about the same rate at which the subject exhales. Since the subject is unaffected by pressure changes in the collection line beyond the bag, it is necessary to use large diameter tubing and valve openings only from the mask to the bag.

The water traps are immersed in cooling baths of dry ice in a 1:1 mixture of CCl_4

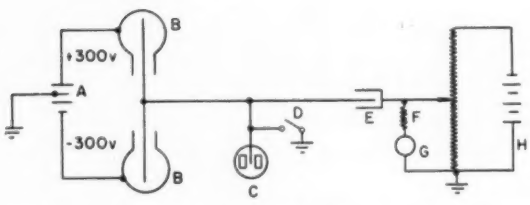

FIG. 2. Schematic diagram of Cambridge Precision Ionization Meter. (*A*) 300 v batteries; (*BB*) dual ionization chambers; (*C*) electrometer; (*D*) grounding key; (*E*) comparison condenser; (*F*) 150,000 ohm precision resistor; (*G*) ammeter; (*H*) variable voltage supply. (Diagram adapted from drawing No. SK-8440 in instruction book of Cambridge Instrument Co., Inc., New York, N. Y.)

and $CHCl_3$. The first trap prevents condensation of moisture in the polyethylene bag, and the other water traps complete removal of water. The Ascarite container is required only for samples which are to be measured in the proportional counter; it is not necessary to remove CO_2 when the ionization chamber method is used. The charcoal trap is also immersed in a cooling bath, because, as will be shown later, radon is not satisfactorily removed from a stream of air by charcoal at room temperature unless large amounts of charcoal are used.

In operation, the large three-way stopcock (*A*) is open to the room while the mask is fitted and, if necessary, while the subject breathes radon-free air previous to sampling. With the subject breathing regularly, the stopcock is opened to the collection line and a stopwatch started simultaneously. At the end of the run the patient's breath is again directed into the room and the clock stopped. The bag is then pumped empty to complete the sampling. The volume of breath collected is measured by the wet test meter in order to correct for the amount of radon in inhaled air and to detect variations in the minute volume. The bag and the line may be flushed with breath or with tank air prior to sampling by means of the by-pass line.

III. MEASUREMENTS OF RADON

Most of the measurements of radon were performed with Cambridge Precision Ionization meters (Failla design), two of which were used. As shown in the diagram (Fig. 2), the instrument employs dual ionization chambers to reduce the effect of background. The electrometer is affected only by the difference in current between the sample chamber and an identical chamber containing inert nitrogen. The original equipment was modified by the substitution of two shielded 300 volt "B" batteries for the power supply unit furnishing the chamber potential. This change improved the stability of the instruments. Since the response of the ionization chamber is not effected by small changes in gas composition, the main precaution to be observed in transferring radon from the charcoal trap to the chamber is to remove water vapor. The transfer system consists of a bubbler for the flushing gas, furnace, coil-type water trap immersed in a dry ice cooling bath, manometer, vacuum pump, and a connection to the chamber. The charcoal trap is opened slowly to the evacuated system and heated to 500° C.; while maintaining the elevated temperature, the trap is flushed with dry aged nitrogen until the system reaches atmospheric pressure. The ionization chamber is then ready to be connected to the electrometer. For calibrations with standard radium solutions or measurements of other liquid solutions, a flask fitted with a bubbler tube and reflux condenser is substituted in place of the charcoal trap and heated by a mantle. Each chamber has a volume of 2 liters as compared with 40 cc. space in the transfer line, 60 cc. space in the charcoal trap, and approximately 100 cc. space in the flasks containing liquid solutions.

The instruments were calibrated with radon from aliquots of a solution of Ra^{226} which had been standardized by the National Bureau of Standards and checked at this laboratory by evaporating small portions on platinum plates and counting alpha particles in a windowless alpha counter. Table 1 summarizes calibrations with four standards prepared from the National Bureau of Standards radium solu-

TABLE I

CALIBRATION DATA FOR ELECTROMETERS

Solution	Activity $\times 10^{-11}$C Ra^{226}	Type of Transfer	Number of Measurements	Ionization Current $\times 10^{-13}$ amp	C/amp
NBS 1	8.00	Direct	10	1.09 ± 0.04	734
		Off charcoal	7	1.09 ± 0.02	734
NBS Stock 1	8.00	Direct	3	1.05 ± 0.01	762
		Off charcoal	10	1.05 ± 0.05	762
NBS 2	4.00	Direct	7	0.53 ± 0.03	755
		Off charcoal	10	0.55 ± 0.02	728
NBS Stock 2	4.00	Direct	3	0.54 ± 0.02	741
		Off charcoal	9	0.53 ± 0.04	755

tion by two different groups. These measurements were made over a period of two years using both electrometers, by adsorption followed by desorption from charcoal as well as by direct transfer from solutions, and by having five persons perform the transfers and measurements.

Values of the ionization current were calculated by the relation $I = C\Delta V/\Delta t$, where C is the value of the added capacitance in farads, and ΔV is the change of potential (volts) in Δt sec. The smallest value of C used in these measurements was $1\mu\mu$F. and the distributed capacitance of the instrument is negligible with respect to this quantity. The calibration factor of 748 curies of radon per amp may be used for other capacitors after they have been calibrated with respect to two used for the radon calibration measurements. It has been convenient to use an exterior source of gamma rays to produce a reproducible ionization rate in the chambers for calibrations of the capacitors where necessary.

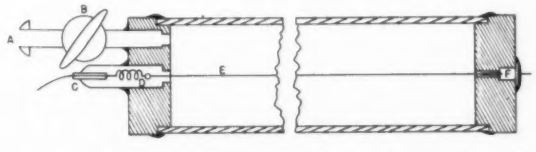

FIG. 3. Proportional counter for radon. (*A*) 18/7 semiball standard taper joint; (*B*) 2 m/m oblique bore vacuum seal stopcock; (*C*) 1/16″ diameter Kovar tubing sealed to pyrex tube; (*D*) 0.016″ diameter phosphor bronze spring; (*E*) 0.005″ diameter copper wire; (*F*) Stupakoff seal No. 95.2004; ▨ stainless steel cylinder (15″ long, 2″ O.D.); ▧ lucite; ■ Apiezon W. cement.

The background current with no shielding and with the instruments in the laboratory was approximately 5×10^{-16} amp. This corresponds to about 0.4 micromicrocuries of radon.

Radon was also measured with proportional counters (Fig. 3) consisting of a cylindrical shell of brass or stainless steel about 15″ long and 2″ in diameter and provided with an anode of 5 mil copper wire insulated at each end by lucite end caps. The construction closely followed models described by Engelkemeir *et al.*[5] A commercial instrument (Nuclear Measurement Corporation Model PC 1) was adapted to supply the necessary recording circuits. The amplifier and pulse height selector were removed from the original chassis and mounted on the metal box used as the electrical shield of the counter whereas the high voltage was brought out from the chassis by a shielded cable to an RC filter placed in the amplifier housing.

With argon as a counting gas at a pressure of one-third of an atmosphere, the counting rate vs. voltage curves showed plateaus for alpha-counting extending from about 1050 volts to 1150 volts with a rise of 5 to 7 per cent for 100 volts. Counters made of stainless steel had backgrounds of about 0.15 counts per minute when new, while brass counters had backgrounds ten times greater. The smaller counting rate corresponds to 0.05 $\mu\mu$c. of radon. Use of high level radon samples resulted in in-

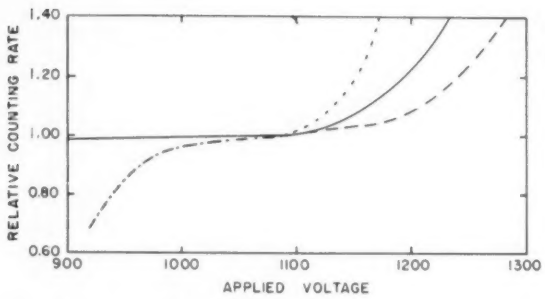

Fig. 4. Typical curves of counting rate *vs* voltage for proportional counter with argon filling at 23 cm. Hg. — — — radon; – – – radon with external source of gamma rays (1.00=280 cpm); ——— plutonium alpha-ray source.

creased backgrounds from RaF deposited in the counter walls.

Since it was impractical to make plateau runs on each counter filling for small counting rates, an auxiliary source of alpha rays was tried as a means of providing large counting rates during plateau runs. The source (Pu^{239}) was placed in a tube which was sealed around a hole in the wall of a counter, and alpha rays were admitted to the counter or blocked off by means of a shutter. However, this device proved unsatisfactory because more uniform pulses were obtained from the localized source of plutonium than from radon. Plateaus with the former began at lower voltages and had much smaller slopes than those for radon (Fig. 4), irrespective of whether the source was mounted on the end of the counter, as in earlier models,[15] or on the side.

A better criterion for choosing the proper counting voltage was obtained through the use of a large source of gamma rays laid next to the counter. As seen in Figure 4, the presence of the gamma-ray source caused a sharp rise in the counting rate near the middle of the plateau obtained with radon alone. By setting the counting voltage somewhat below this point reproducible results could be obtained. In practice, short counts at 25 volt intervals were taken with radon in the counter and the gamma-ray source nearby until the counting rate rose sharply; then the gamma-ray source was removed, and the radon was counted at the last voltage setting previous to the increase. With this procedure, the proper voltage could be determined in less than one-half hour.

Before transferring radon from a charcoal trap to a proportional counter, the charcoal trap is removed from the adsorption line, placed in an ice water bath, and flushed with about 2 liters of argon in order to remove air from the trap. The charcoal trap is then attached to a vacuum line, heated to 500° C., and the desorbed radon transferred to the counter by means of a Toeppler pump. Additional small increments of argon are added to the trap as a flush until the pressure in the counter rises to about 23 cm. Hg. This combination of heating, flushing, and evacuating quantitatively removes the radon from the charcoal. The stopcocks on the trap are then closed and the charcoal is ready for another sample.

After being filled, the counter is allowed to stand three hours for RaA and RaC′ to grow into equilibrium with the radon before counting is started. A positive potential of 900 volts is applied to the center wire during this period in order to obtain a reproducible distribution of the daughter nuclides. Practically all of the alpha rays from gaseous Rn would be expected to be counted, but the decay products (RaA and RaC′) presumably become attached to the walls of the counter where only half of their disintegrations result in alpha rays being directed into the electrical field of the

Table II

Efficiency of proportional counter as determined by aliquoting of radon from a NBS solution of Ra^{226} into the counter. Errors indicated are the statistical 0.9 error in counting

Sample	μμc. Rn^{222}	Cpm	Cpm/μμc. Rn
1	36.1	150±2.3	4.16
2	34.4	143±2.0	4.16
3	54.7	219±4.2	4.00
4	30.7	127±3.0	4.16

counter. Accordingly, 1 $\mu\mu$c. of Rn in equilibrium with RaA and RaC′ was expected to provide a counting rate of 4.44 alpha counts per minute (cpm) as a maximum. Table II presents the counting rates obtained when known amounts of radon from a National Bureau of Standards radium solution were introduced into a counter. On the average, 93 per cent of the postulated maximum rate was obtained.

IV. RECOVERY OF RADON FROM BREATH

In order to test the recovery of known amounts of radon mixed with breath and passed through the collection apparatus, the radon dispenser illustrated in Figure 5 was used. Known amounts of radon from sealed glass flasks containing aliquots of a National Bureau of Standards radium solution were transferred to the dispenser by the following procedure: (1) stopcocks (*A*) and (*B*) were opened so the neoprene balloon (*C*) was collapsed but contained air at atmospheric pressure; (2) stopcock (*A*) was closed and the glass bulb (*D*) was evacuated through (*B*); (3) radon was flushed out of the radium solution into the glass bulb by slowly bubbling argon through the solution and through a water trap into the bulb; (4) stopcock (*B*) was closed after atmospheric pressure was reached in the bulb. The glass bulb was then attached by means of the ground glass joint (*E*) to the collection apparatus at a point between the face mask and the first water trap. After the subject started breathing into the apparatus, the stopcocks of the dispenser were opened and N_2 passed slowly through stopcock (*A*) into the balloon which expanded, forcing radon into the stream of breath. The rate of N_2 flow was adjusted so as to empty the glass bulb in slightly less than the period of time desired for the test; then the balloon was deflated and inflated rapidly to flush residual radon from the bulb into the collection line. Use of this dispenser allowed introduction of radon into the collection line at a much more uniform rate than if radon had been flushed from a glass bulb by a direct stream of gas. Recovery of radon from the dispenser was found to be complete even after three days in contact with the rubber balloon inside the dispenser.

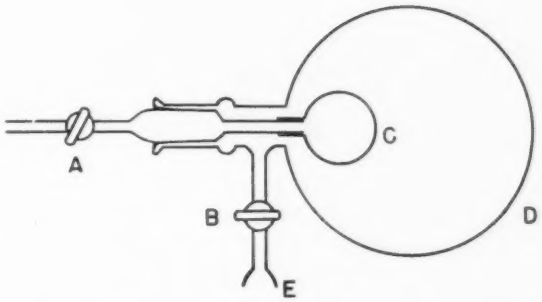

FIG. 5. Flask for continuous introduction of radon into a stream of breath. (*A*) (*B*) stopcocks; (*C*) neoprene balloon; (*D*) 2 liter glass flask; (*E*) semi-ball ground glass joint.

TABLE III

RECOVERY OF KNOWN AMOUNTS OF RADON MIXED WITH BREATH AND COLLECTED ON CHARCOAL

Run	$\mu\mu$c. Rn^{222}	Length of Run (min.)	Vol. Breath (BTPS liters)*	Cpm Obtained / $\mu\mu$c. Rn
1	123	16	142	3.90
2	93.5	30	207	3.53
3	145	30	199	3.81
4	1.32×10^3	15.5	146	3.28
5	10.0×10^3	20	131	3.69
			Average†:	3.64 ± 0.24

* Volume calculated at 37° C. and ambient pressure, saturated with water vapor.

† Mean value ± standard deviation of a single measurement.

Table III gives the recoveries of radon which were obtained using the gas dispenser and the collection line. Runs 1 through 4 were obtained using gas which had been counted to determine the number of micromicorcuries of radon present and then transferred from the counter to the glass bulb of the dispenser. This procedure was more convenient than direct flushing from a generator. Run 5 was obtained using direct flushing of a radon generator into the dispenser. All data are corrected for decay. The degree of reproducibility of the

TABLE IV

RETENTION OF RADON ON CHARCOAL

A. Stock supply of radon mixed with air; flow rate of 8.5 liters/min.; charcoal traps connected in series

Run	BTPS Liters*	Charcoal Traps†				cpm (a+b) per liter
		First		Second‡		
		t° C.	cpm, a	cpm, b	Per cent of total	
1	56.2	−80	1.40×10^4	50	0.35	256
2	160	−80	3.98×10^4	269	0.67	251
3	272	−80	7.09×10^4	824	1.15	253
4	610	−80	14.6×10^4	3.10×10^3	2.03	246
5	19.8	+30	—	2.19×10^3	43	—
6	39.2	+30	—	6.83×10^3	68	—
7	59.0	+30	—	1.06×10^3	7.0	—

* Volume calculated at 37° C. and ambient pressure, saturated with water vapor.
† Each trap contained 7 grams of charcoal except for the first trap to Run No. 7 which contained 47 grams.
‡ For each run the second trap was at −80° C.

B. Radon absorbed on charcoal, then eluted with nitrogen; flow rate of 2.4 liters/min.; 7 grams of charcoal at 30° C.

BTPS Liters	Per cent of Rn left in trap after elution
3	100
4	95
34	56
39	38
39	43
64	19

runs is indicated by the values of the fifth column which lists the ratios of cpm obtained to $\mu\mu$c. of radon used. The standard deviation (6 per cent of the average value) reflects variations in all parts of the procedure: aliquoting, collection of radon on charcoal, transferring to the counter, and errors in counting. The average value of 3.64 for the ratios is 11 per cent less than the 4.12 cpm/$\mu\mu$c. Rn (*cf.* Table II) which would have been obtained if all the radon were recovered. Six per cent of the gas is left in the Toeppler pump, the manometer, and the vacuum line connections when radon was transferred from charcoal to the counter, and other sources of loss of radon are indicated below.

The retention of radon on charcoal for collection periods of different durations was studied using an evacuated gas cylinder to which 5×10^{-7} curies of Rn were added from a solution of radium. The cylinder was then filled with air to a pressure of 2,000 lb. per sq. in. This provided the equivalent of 6,700 liters of air at STP which contained radon with a calculated concentration of about 270 cpm per liter. Gas from this cylinder was passed through the collection line of Figure 1 to which was added a second charcoal trap in series with the first. By using a large amount of radon for each run, measurement of radon found in the second trap provided a sensitive means of determining the fraction of radon not retained in the first trap. Table IVA summarizes information obtained in this

manner on several variables affecting retention of radon.

It is apparent that although retention of radon was almost quantitative for a thirty minute run (at 8.5 l/min.) using the conditions adopted for analyses, the fraction of unretained radon increased steadily with increases in total sample volume. On the other hand, increasing the amount of charcoal in the trap reduced the fraction of radon lost. The data of Table IVA also indicate that charcoal at room temperature retained radon so inefficiently that a large amount of charcoal was necessary for quantitative work. This is further brought out by Table IVB which shows that radon previously adsorbed on charcoal was readily eluted by a stream of nitrogen when the charcoal was at room temperature.

As described earlier, use of the proportional counter required that the charcoal trap containing collected radon be flushed with the counting gas in order to obtain a pure gas for counting. To determine whether radon was lost in this step, a trap containing 3.6×10^4 cpm of radon on charcoal was allowed to stand ten hours at room temperature, then cooled in an ice-water bath and flushed with 2.5 liters of argon which was collected in an ion chamber. The activity in the ion chamber was 0.9 per cent of the total activity on the charcoal.

The procedure for recovering radon from charcoal by heating to 500° C. was considered satisfactory since additional flushing and heating of the charcoal until it glowed resulted in no further recovery of activity (less than 0.5 cpm) after the standard procedure had removed 4.85×10^3 cpm of radon from a charcoal trap used for a test run.

Radon may also have been lost in the Ascarite trap,[14] in the polyethylene bag, in water frozen out in the water traps, and in stopcock grease. However, consideration of the over-all recovery of radon and the efficiency indicated above for collection on and removal from charcoal indicates that no single source of error is large.

V. APPLICATION TO BREATH MEASUREMENTS

The techniques described above for measuring radon in breath have been used to date for studies of radium retention at levels of the order of 1 microgram. The most extensive of these[21] dealt with 19 patients at the Elgin State Hospital who had been injected with from 70 to 450 μg. of Ra^{226} in 1931.[24] Analyses were made in 1951 and repeated two years later on 13 of the patients who had radium burdens ranging from 0.5 to 3 μg. The average difference between the two sets of radon analyses was 11 per cent, excluding 1 patient for whom the analyses differed by a factor of two. The fraction of radon exhaled was found to be 70 per cent. This is considered to be in agreement with the work of Evans,[6] since the average breathing rate was 7.5 l/min. instead of 5 l/min. as assumed by Evans.

A study[17] was also made on several subjects who had inhaled radium sulphate dust in industrial accidents. The variations of the fraction of radon exhaled were followed, and measured decreases in body radium were compatible with the amount of radium found to be excreted.

At present, adsorption of radon on charcoal as a means of extending analyses to extremely small concentrations of radon in breath is being investigated for use in measuring the radium content of living subjects with no known exposure to radium. The nature of the problem is briefly considered here by comparing the amount of radon released by body radium with the amount expected from sources of contamination.

The average radium content of cadavers analyzed by Hursh and Gates[13] at Rochester, New York, was 1.18×10^{-10}g. On the assumption that 70 per cent of the radon from fixed body radium is exhaled[21] it is readily calculated from Equation (1) that persons with this amount of radium would exhale about 0.01 μμc. Rn per minute, or less than 2×10^{-3} μμc. per liter. A measurable quantity of radon can be readily accumulated from breath of even this low

concentration by sampling for many minutes, but, as will be shown below, the amount of radon from room air and from materials used in the analysis is so large that such small radium burdens could be measured only with extraordinary precautions. However, larger radium burdens should be present in populations whose water or food contains a larger concentration of radium than that of the subjects analyzed by Hursh and Gates. This may be the case for people in a number of suburbs close to Chicago whose water (from deep wells) contains more than 3 $\mu\mu$c. Ra per liter[25] as compared to less than 0.05 for Rochester or New York City.

Room air contains about 0.2 micromicrocurie of radon per liter on the average, and some of this radon is absorbed by the body through respiration. Thus, radon-free air must be supplied to the subject not only during a sampling period but for some time prior in order to reduce the concentration in expired air or radon originally derived from inhaled air. Using the data of Harley and co-workers[8] on elimination of inspired radon and extrapolating to saturation uptake by means of equations derived for other rare gases,[26] it is estimated that after one hour of breathing radon-free air the concentration of radon in expired air would be reduced to about 2 per cent of that in room air and that another four hours would be required to reach 1 per cent. The latter figure would correspond to 2×10^{-3} $\mu\mu$c. per liter of radon previously absorbed from room air of the above concentration, and as much radon would be collected from this source as from body radium at the level reported by Hursh and Gates.

Furthermore, air compressed in steel cylinders may continue to have an appreciable concentration of radon even though allowed to age for many half-lives of radon. Analyses of air from a dozen or more full cylinders at this laboratory have shown radon concentrations of from 5×10^{-4} to 5×10^{-3} $\mu\mu$c. Rn per liter of air (STP) two months after filling. The radon evidently emanates from radium in the cylinder or cylinder walls so radon is continually formed in the cylinder, and air from a partially emptied cylinder has a larger concentration of radon than air taken when the cylinder is full. For example, air from a cylinder was found to contain 0.12 $\mu\mu$c. Rn in 250 liters (STP) when the gauge reading was 220 cu. ft., the cylinder was then jetted until the reading was 32 cu. ft.; twenty-two days later another analysis showed 0.68 $\mu\mu$c. Rn in the same volume. Thus, the concentration of radon was inversely proportional to the volume of air in the cylinder.

The charcoal used here (6–14 mesh activated coconut charcoal, Burrel Co., Pittsburgh, Pa.) was found to contain 0.013 $\mu\mu$c. Ra per gram. Accordingly, for analyses of small radium burdens, the amount of charcoal used for each run should be kept small, for it may not be feasible to de-emanate the charcoal immediately before use and to remove the radon soon after each sample is collected. As noted before, the length of the sampling period and the temperature of the charcoal are important in determining how much charcoal must be used for satisfactory retention of radon. It has also been found that less charcoal may be used if carbon dioxide is removed before the adsorption step. Only 70 per cent of the radon was retained by 7 grams of charcoal from breath samples of thirty minutes' duration when carbon dioxide was not removed, while retention on 20 grams of charcoal was satisfactory. However, the advantage of using smaller amounts of charcoal may be more than offset by radon contamination from absorbents used to remove carbon dioxide. Ascarite was found to release about 0.07 $\mu\mu$c. of Rn per liter of carbon dioxide absorbed, corresponding to about 0.4 $\mu\mu$c. of Rn for a thirty minute breath sample. Since Ascarite is a mixture of asbestos and NaOH, it was hoped that NaOH alone might contain less radium, but a sample of reagent grade NaOH was found to contain 0.05 $\mu\mu$c. Ra/g. and 1.1 $\mu\mu$c. Rn was obtained from the solid reagent when used to remove carbon dioxide from the equivalent of a thirty minute breath sample. In experi-

ments with the less convenient procedure of passing air through de-emanated solutions of caustic, blanks of less than 0.05 $\mu\mu$c. Rn have been obtained using air-carbon dioxide mixtures equivalent to 200 liters of exhaled air. This procedure removed enough carbon dioxide to permit use of the low-background proportional counter.

Preliminary results with subjects breathing radon-free air for twelve hours or longer indicated that a body content of the order of 10^{-10} gram Ra may be detected by refining the procedure along lines suggested by the above discussion. For this work the supplied air was passed through charcoal in order to remove radon, and carbon dioxide from exhaled air was absorbed by a solution of KOH.

VI. SUMMARY

Equipment and procedures are described for measuring the time rate of elimination of radon in exhaled air. The accuracy and sensitivity of the analysis are improved by sampling large volumes of exhaled air from which radon is adsorbed on charcoal. Interference with normal breathing is negligible, because subjects breathe through large diameter tubing into a flexible bag from which the sample is drawn through the collection apparatus under a small vacuum. Sampling periods of thirty minutes' duration are common. The radon is measured in a low background proportional counter or in an ionization chamber which is connected to an electrometer. The feasibility of extending radon analyses to normal body burdens of the order of 10^{-10} gram Ra is discussed.

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STUDIES OF THE METABOLISM OF RADIUM IN MAN

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INTRODUCTION

SINCE the advent of nuclear reactors, the ever increasing use of radioactive isotopes has demonstrated the practical necessity for a clear understanding of the metabolism of the various elements in man. Such information is essential to the establishment of realistic values for permissible concentrations of radioactive elements deposited in the body as well as to provide a basis for therapeutic removal. The long-lived radioelements that deposit in bone present a particularly difficult problem, since they have thus far proved refractory to efforts to accelerate their normal low rate of excretion.

Following the early observations of Blum,[5] Hoffman,[13] and Martland[28] in 1924 and 1925, who showed that internally deposited radium and mesothorium produce severe necroses, there have been several reports of the clinical course of radium poisoning.[2,6,20,25,26,27,29,34,42] Radium has been shown to be retained tenaciously by bone[1] in which its distribution remains highly heterogeneous during the entire lifetime of the host.[12,22] It is excreted so slowly that its presence in the body may be readily detected many years after a significant initial exposure. Experiences with radium poisoning in man during the last thirty years provide the only good information on the long term effects of radioactive elements deposited in the human skeleton and consequently form the primary basis for the estimation of tolerable concentrations of bone-seeking isotopes in general.

The earliest cases of radium poisoning were observed among employees of the luminous dial painting industry,[28] where the now long-outmoded practice of tipping the brush in the mouth was responsible for the ingestion of dangerous quantities of radioactive paint. This source of patients, however, did not provide clear cut instances of poisoning with radium alone, since the luminous paint contained mixtures of mesothorium (Ra^{228}), radiothorium (Th^{228}), and radium 226. Because of the relatively short half-lives of mesothorium (6.7 years) and radiothorium (1.9 years) and the complexity of their decay schemes, it has been difficult to obtain proof of their original proportions sufficient to assess their contributions to the total biological damage produced.[2]

Since radium was regarded as a useful therapeutic agent until about twenty years ago, it is still possible to find significant numbers of people who were given radium orally or intravenously. It is generally assumed that the Ra^{226} given these people was relatively free from mesothorium and radiothorium contamination.

There exist only a few scattered observations which pertain to the quantitative metabolism of radium in humans. These have been summarized by Silberstein[40] and by Aub *et al.*[2] Although it is possible today to find persons with appreciable radium burdens, there is usually no means of determining the original dosage, and other circumstances surrounding the administration often remain obscure. Therefore, it is especially significant when a group of subjects with a known history of radium administration is found.

In 1931, a selected group of patients in the Elgin State Hospital, Elgin, Illinois, mostly dementia praecox cases, were each given multiple intravenous injections of radium chloride (10 micrograms radium element per dose) at weekly intervals over periods ranging from two to six months. This study, reported by Schlundt, Nerancy and Morris,[37] is almost unique in that the dosages were recorded and the patients were measured for radium retention on two

separate occasions within the first year. Nineteen of the original 32 patients were located in 1951 and studied for clinical symptoms and for radium content. In addition, several other persons who had received radium injections have been located in the Chicago area and likewise studied. This report deals with the results of these physical determinations and attempts to draw conclusions concerning the long term metabolism of radium in humans. The results of clinical studies of these patients will be described in another article.[21]

BASIS FOR MEASUREMENT OF RETAINED RADIUM

Radium 226 is a naturally radioactive element with a half-life of 1,620 years. Inspection of its decay pattern shows that in disintegrating it is converted to radon, a radioactive noble gas, having a half-life of 3.825 days. Radon is produced by radioactive decay of its parent at an essentially constant rate of 2.097×10^{-12} curies per second per microgram of radium.

Since the noble gases cannot participate in chemical reactions, a considerable fraction of the radon is removed from the site of production (bone) by the processes of diffusion and dissolution in body fluids. The work of Tobias *et al.*,[43] Behnke and Willmon,[4] and Lange and Evans[18] indicates that minor losses of radon from the body probably occur by way of the skin and intestinal tract. Practically all of the radon elimination from the body is by way of the lungs and, with proper instrumentation, this radon may readily be measured in the expired air. Thus, with any constant set of respiratory conditions maintained for a sufficient time, each 2.097×10^{-12} curies exhaled per second represents the contribution of 1 microgram of radium. The accuracy obtainable in estimating the quantity of radium that contributes to expired radon is limited almost entirely by the ability of the method of collection of expired air to obtain specimens representative of the rate of exhalation of radon averaged over periods of time large compared to its half-life. Unpublished work of the authors, in dogs injected with radium, shows that both the concentration of radon in the expired breath and the quantity expired per unit time may be altered appreciably by changes in respiratory activity. Thus, in practice, the deviations in individual determinations of radium, as represented by expired radon, may be considerable.

The fraction of radon retained in the body decays radioactively through several successive, short-lived, radioactive daughters. This decay process is accompanied by the emission of gamma rays which, by appropriate instrumentation, may be measured externally to the body.

The total radium content of a living subject, therefore, is determined as the sum of these two completely independent measurements.

DISCUSSION OF EARLY WORK OF SCHLUNDT *et al.*

The early determinations of radium retention in the Elgin Hospital patients were made using the best techniques and equipment available in 1931–1932. These measurements of expired radon and externally detectable gamma rays are described in the original paper of Schlundt, Nerancy and Morris.[37] Since approximately twenty years have elapsed between the early work of these authors and the recent measurements reported herein, it is well to examine the available information to determine the degree of over-all consistency and reliability. It may be stated at the outset that the authors have concluded that the early work of Schlundt *et al.* was essentially accurate, although it has been impossible to determine the error involved in individual measurements. In this evaluation, it should be indicated, considerable weight has been placed on Schlundt's reputation among his associates as an extremely thorough, careful worker with wide experience in working with radium. The following items appear to be worthy of individual consideration:

1. Was the original measurement of

ampoule content correct?

2. Did the patient receive the full content of the ampoule or was a significant percentage lost by adsorption onto the glass surfaces of the ampoule and syringe?
3. Were the radium preparations contaminated with mesothorium?
4. What degree of accuracy was attained in measurements of retained radium using the two complementary techniques for determination of retained and exhaled radon?

These questions will be covered separately.

From the files of the late H. H. Barker, a vice-president of the United States Radium Corporation, it was ascertained that the radium used for the Elgin Hospital patients was supplied by the U. S. Radium Corporation through an identified Chicago outlet. This radium was supplied in sealed glass ampoules, each of which was labelled to contain 10 micrograms of radium element (as the chloride) in 2 milliliters of sterile isotonic NaCl solution. Through the kindness of Dr. M. Williams of the Mayo Clinic and Mr. G. Ferlazzo of Memorial Hospital, New York City, it was possible to obtain seven such ampoules (originally prepared by the U. S. Radium Corporation) which had been retained unopened for about twenty-five years (Fig. 1). These ampoules were measured (without being opened) for radium content in a pressurized, gamma-ray ionization chamber which had been calibrated against National Bureau of Standards radium preparations. The results are presented in Table 1. It will be

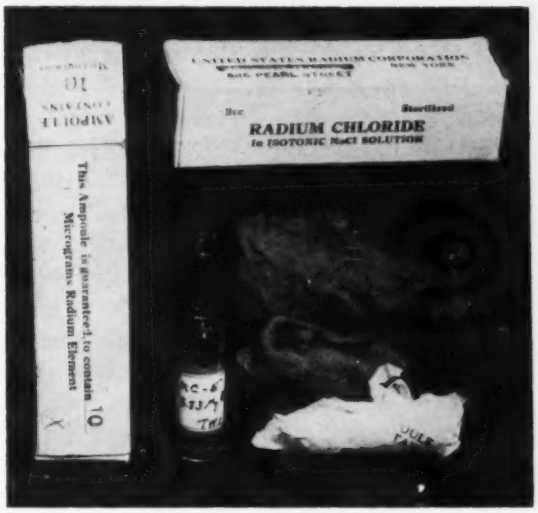

Fig. 1. Ampoule of $RaCl_2$ originally prepared about 1928 for intravenous injection. Label on ampoule was added by the authors.

Table I

Measurements of $RaCl_2$ ampoules prepared for intravenous administration about 1928

Ampoule (No.)	Total Ra Content (μgm.)	Per Cent of Measured Ampoule Content			MsTh, 1953* (per cent)
		Retained in ampoule	Retained in syringe	Delivered from syringe	
MC-4	9.16	1.96	2.62	95.20	
MC-5	8.83	27.41	4.64	66.02	.05 ± .03
MH-1	9.00	0.44	2.22	97.44	.05 ± .03
MH-2	8.99	1.00	3.56	95.33	
MH-3	18.15†	1.05	3.14	93.94	
MH-4	9.00	1.11	2.78	96.00	
MH-5	8.31	1.68	2.89	96.03	
Average	8.93	1.21‡	2.87‡	95.66‡	

* Per cent MsTh is calculated as $\frac{\mu cMsTh}{\mu cMsTh + \mu cRa} \times 100$.

† 20 μgm. ampoule—treated as two 10 μgm. ampoules in averaging.

‡ Mc-5 not figured in averages.

noted that the radium content of these ampoules was close to 9 μgm. in every case.

The ampoules were then opened and the solutions withdrawn, with separate 2 ml. Ideal syringes fitted with B-D No. 22 1 inch needles, using techniques calculated to duplicate hospital methods and not to deliver quantitatively. The syringes were emptied into new Pyrex ampoules which were then sealed off as were the original empty ampoules. The syringes and needles were placed directly into glass tubes which were then sealed. After an appropriate period to allow radon equilibration the radium contents of the three parts were measured as before. The results (Table 1) indicate that, with one exception, after twenty-five years the radium salt was essentially quantitatively in solution and that *96 per cent* of the total radium was delivered from the syringe.

Since the quantities of radium in these ampoules were only 90 per cent of the stated content, it was particularly important to determine whether this discrepancy could be attributed to the decay of an initial mesothorium contaminant. The assay of residual mesothorium in two of these ampoules (Table 1) was accomplished through the kindness of Dr. C. E. Miller and Mr. R. E. Rowland, of the Radiological Physics Division of this Laboratory, who have devised an ingenious method of determining MsTh in the presence of large amounts of Ra by measuring the delayed coincidences of the ThC β particle and the ThC′ α particle. This method will be published in detail elsewhere. The results of the measurements indicated that, in 1953, the MsTh content was no more than 0.05 per cent, a value which is so near the present limiting sensitivity of the instrument that it should only be regarded as an upper limit.

The half-life of mesothorium (6.7 years) is such that a given quantity of MsTh will be reduced to 7.5 per cent of its initial value in twenty-five years. Therefore, the initial MsTh contamination in these ampoules could not have exceeded 0.66 per cent, a negligible quantity.

Further evidence of the absence of MsTh contamination in the radium preparations used in the Elgin Hospital study is supplied by the fact that earlier publications by Schlundt *et al.*[35] described the detection of thoron, an isotope of Rn produced through decay of MsTh, in the expired air of persons containing MsTh. Since the apparatus was essentially the same in both studies it is probable that the presence of significant quantities of MsTh and its daughters would have been detected in the Elgin study.

Another such indication is that shipments of radium from the U. S. Radium Corporation to retail outlets, including the Chicago vendor of interest here, were accompanied by a certificate which stated, "The gamma radiation from this preparation is due entirely to radium and its derivatives and not to mesothorium or any of its disintegration products."

As mentioned above, it has been impossible to determine the error in individual determinations which may have been present in the early work of Schlundt, Nerancy and Morris.[37] However, certain observations which indicate the results were generally correct are presented in the following text. As stated in their original paper, the calibration of the Wulf-Hess electrometer used for determining the nonemanating radium fraction was based upon the results of Ives, Knowles and Britten[17] who used a duplicate instrument. These authors, in addition to working against known radium sources, checked their calibration against radon seeds implanted in a cadaver in proportion to skeletal mass. They also made observations of the rate of fall of their electrometer fiber produced by radium sources at fixed distances and determined that a radium source placed 37.4 cm. from the instrument produced the same reading as an equivalent amount of radium distributed in a cadaver under their conditions of measurement. Schlundt, Nerancy and Morris repeated these measurements of sources using their own instru-

ment and determined the ratio of sensitivity of their instrument to that of Ives *et al.* to be 1.19. Their calibration constant of 180×10^{-6} div/sec/microgram Ra in the patient is to be compared to 151×10^{-6} obtained by Ives and to 85.7×10^{-6} reported by Schlundt, Barker and Flinn in 1929.[35] The latter value was obtained from postmortem measurements of the body of a woman who had worked as a dial painter. This value was not used by Schlundt in the Elgin study presumably because of the high probability of enough mesothorium in the cadaver to invalidate the result with respect to radium. As a commentary on the determination, it may be pointed out that at the time of the early measurements, nonexhaled radon represented a rather small fraction of the total radium and therefore relatively large errors would have been of small significance in the final value for total radium content.

The greater part of the total radon in Schlundt's measurements was found in the expired air. This exhaled radon was measured using a Lind electrometer with ionization chambers calibrated directly against radon from known radium solutions.

The largest source of error probably arose from the use of an assumed average respiratory volume of 7.5 liters per minute for all patients. Thus a concentration of $2.097 \times 10^{-12} \times 60/7.5 = 16.8 \times 10^{-12}$ C Rn/liter was taken to represent 1.0 μgm. of Ra element in the patient. It is apparent that the actual mean radon concentration will be inversely proportional to the true minute volume. However, it is noteworthy that the average minute volume assumed in this early work is identical with the average measured in all patients in the current study. Furthermore, the spread in retention for the group was no greater in Schlundt's measurements than obtained by us after twenty years.

It should also be noted that the ratio of expired to nonexpired radon in Schlundt's measurements was quite constant at each of the two intervals where determinations were made. At the time of the first measurements the average percentage of the retained radium appearing as expired radon was 88 per cent and six months later was 84 per cent. The measurements made by the present authors showed this value to be about 70 per cent after twenty years. Since all experience,[40] as well as unpublished data (*vide infra*) of the present authors obtained from dogs in which this factor was specifically studied, shows that the maximum percentage exhalation of radon occurs at the earliest times after injection and decreases thereafter, it follows that the early values of Schlundt should have been in excess of later values, as is borne out by the combined data compiled in Table II.

This review of the early work with the Elgin Hospital patients reveals no reason to suspect any major source of error. Examinations of radium ampoules prepared for injection about 1928 indicate that in the Elgin study about 4 per cent of the intended dosage may have been lost in the syringe and ampoule and that the actual radium contents of the ampoules may have been about 10 per cent lower than the intended amount. However, these findings can be regarded as little more than indications and in view of lack of more detailed information about the early work, no correction for these possibilities has been applied.

MEASUREMENTS IN THE CURRENT STUDY

In an effort to reduce sampling errors caused by variations in respiratory activity, in the determination of expired radon, a method was devised in which all the radon expired in a period of twenty minutes was quantitatively adsorbed at low temperature on activated coconut charcoal. This technique affords relatively large quantities of radon so that instrumental sensitivity is not a problem and permits measurements of the total volume of gas expired during the sampling. The average minute volume determined in 57 patients was 7.5 liters per minute which is in excellent agreement with the value assumed by Schlundt *et al.*

TABLE II

MEASUREMENTS OF RADIUM RETENTION IN ELGIN HOSPITAL PATIENTS

	Patient	Sex	Age at injection	Injected dose μgm. Ra	Interval from last injection to 1st measurement	R1 First Measurement: % Injected dose as radon	% Injected dose as γ-rays	% Injected dose retained	Rn / Rn+γ	Retention μgm.	R2 6 Months after First Measurement: % Injected dose as radon	% Injected dose as γ-rays	% Injected dose retained	Rn / Rn+γ	Retention μgm.	R3 233 Months after First Measurement: % Injected dose as radon	% Injected dose as γ-rays	% Injected dose retained	Rn / Rn+γ	Retention μgm.	R4 258 Months after First Measurement: % Injected dose as radon	% Injected dose as γ-rays	% Injected dose retained	Rn / Rn+γ	Retention μgm.
					Days																				
	A	F	22	150	201	4.80	0.67	5.47	0.88	8.2	1.67	0.60	2.27	0.74	3.4	0.69	0.38	1.07	0.64	1.61	0.77	0.40	1.17	0.66	1.75
	B	M	27	150	201	3.60	0.40	4.00	0.90	6.0	1.87	0.20	2.07	0.90	3.1	0.26	0.07	0.33	0.78	0.50	—	—	—	—	—
	C	F	63	150	201	2.27	0.20	2.47	0.92	3.7	0.94	0.12	1.06	0.87	1.6	0.22	0.06	0.28	0.79	0.42	—	—	—	—	—
	D	F	51	150	201	8.33	0.93	9.26	0.90	13.9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	E	M	29	160	194	7.82	0.81	8.63	0.91	13.8	2.56	0.88	3.44	0.74	5.5	—	0.47	—	—	—	—	—	—	—	—
	F	F	56	160	194	2.31	0.56	2.87	0.80	4.6	—	0.44	—	—	—	—	—	—	—	—	—	—	—	—	—
	G	F	48	160	194	1.81	0.44	2.25	0.80	3.6	0.00	0.19	—	—	—	—	—	—	—	—	—	—	—	—	—
	H	—	—	160	194	2.12	0.25	2.37	0.89	3.8	1.12	0.05	1.17	0.95	1.9	—	—	—	—	—	—	—	—	—	—
	I	F	28	180	180	3.28	0.44	3.72	0.88	6.7	1.00	0.06	1.06	0.94	1.9	0.32	0.11	0.43	0.74	0.78	0.24	0.11	0.35	0.69	0.63
	J	F	31	200	166	2.95	0.15	3.10	0.95	6.2	2.05	0.05	2.10	0.98	4.2	0.33	0.16	0.49	0.67	0.97	0.33	0.12	0.45	0.73	0.90
	K	F	22	200	166	—	0.25	—	—	—	—	—	—	—	—	0.35	0.11	0.46	0.76	0.91	0.35	0.11	0.46	0.76	0.93
	L	F	25	260	124	4.62	0.88	5.50	0.84	14.3	1.27	0.69	1.96	0.65	5.1	1.73	0.83	2.56	0.68	6.65	1.74	0.87	2.61	0.67	6.80
	M	F	—	380	124	—	0.26	—	—	—	—	0.34	—	—	—	—	—	—	—	—	—	—	—	—	—
	N	F	30	360	180	0.50	0.31	0.81	0.62	2.9	1.58	0.25	1.83	0.86	6.6	0.32	0.16	0.48	0.67	1.71	0.33	0.14	0.47	0.70	1.70
	O	F	25	260	23	2.46	0.46	2.92	0.84	7.6	0.92	0.27	1.19	0.77	3.1	0.21	0.15	0.36	0.58	0.93	0.26	0.13	0.39	0.67	1.01
	P	F	23	250	30	2.32	0.44	2.76	0.84	6.9	1.68	0.36	2.04	0.82	5.1	0.64	0.38	1.02	0.63	2.56	—	—	—	—	—
	Q	M	33	450	20	3.58	0.35	3.93	0.91	17.7	—	0.29	—	—	—	0.13	0.05	0.18	0.72	0.81	0.29	0.05	0.34	0.85	1.54
	R	F	32	410	13	—	0.27	—	—	—	—	—	—	—	—	0.56	0.31	0.87	0.64	3.57	0.45	0.30	0.75	0.60	3.09
	S	F	51	70	60	—	0.71	—	—	—	—	—	—	—	—	0.50	0.27	0.77	0.65	0.54	0.62	0.29	0.91	0.68	0.64
	T	F	18	110	30	7.56	0.62	8.18	0.92	9.0	4.36	0.46	4.82	0.90	5.3	0.65	0.25	0.90	0.72	0.99	0.70	0.29	0.99	0.71	1.09
	U	F	28	90	30	—	0.56	—	—	—	—	0.67	—	—	—	0.43	0.21	0.64	0.67	0.58	0.40	0.24	0.64	0.63	0.58
	V	M	23	100	30	6.20	0.30	6.50	0.95	6.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	W	M	—	90	30	9.56	1.22	10.78	0.89	9.7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	X	—	—	90	30	4.33	0.33	4.66	0.93	4.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Rose	D.	F	22	200		4.70	0.85	5.55	0.86	11.1	—	—	—	—	—	0.63	0.28	0.91	0.69	1.82	—	—	—	—	—
Paul	N.	M	23	110		—	—	—	—	—	—	—	—	—	—	0.35	0.07	0.42	0.83	0.46	0.38	0.09	0.47	0.81	0.52
Edith	C.	F	23	260		—	—	—	—	—	—	—	—	—	—	0.19	0.12	0.31	0.61	0.81	—	—	—	—	—
Average						4.45*	0.51	5.00*	0.88*	—	1.75†	0.35	2.08	0.84	—	0.40‡	0.20‡	0.58‡	0.69	—	0.43‡	0.19‡	0.62‡	0.70	—

* Excluding N.
† Excluding G.
‡ Excluding L.

TABLE III

COMPARISON OF BODY RADIUM CONTENT ESTIMATED FROM CONCENTRATIONS IN BONE AND FROM *in vivo* MEASUREMENTS

Patient No.	Body wt., kg.	Estimated wt. skeleton, kg.	Wt. bone specimen, gm.	Ra content of specimen, μgm.	Ra content of specimen μgm. $\times 10^{-4}$/gm.	Estimated Ra content of skeleton, μgm.	Ra content estimated in vivo, μgm.	Source of bone specimen
103 (M.C.) Ra injections	57.5	5.8	22.0	.015	6.82	4.0	5.3	Fragments from acetabulum and head of femur
112 (M.K.) Ra injections	59	5.9	77.2	.038	4.92			Skull
			32.1	.005	1.56			Distal fibula
			72.9	.009	1.24			Tarsal bones (tumorous)
			51.2	.006	1.17			Proximal tibia
			38.9	.002	.52			Ankle bones
			272.3	.060	2.20	1.3	1.2	
118* See also Case 4, ref. 2 Drank Ra water	52	5.2	67.8	.048	7.08			Foot bones
			189.4	.120	6.34			Vertebrae
			204.8	.146	7.13			Femur
			150.3	.041	2.73			Ribs
			612.3	.355	5.80	3.0	10.5*	
302 (I.D.) Dial painter	57	5.7	34.2	.028	8.19			Distal femur
			79.6	.065	8.17			Proximal tibia
			40.3	.021	5.21			Distal tibia
			29.5	.015	5.08			Foot bones
			37.2	.017	4.57			Proximal fibula
			78.9	.035	4.44			Calcaneus
			299.7	.181	6.04	3.4	3.8	
313 (R.W.)	43.6	4.4	72.0	.010	1.30			Fibula
			107.4	.014	1.39			Tibia
Dial painter			179.4	.024	1.34	0.6	1.3	

* In vivo measurement in 1941 by Aub, Evans, Hemplemann and Martland.[2]

The adsorbed radon was removed from the charcoal by heating and flushed into one of a dual set of ionization chambers, connected to a Lindeman-Ryerson electrometer (Failla's design—purchased from the Cambridge Instrument Co., Grand Central Terminal, N. Y.). The instrument had been previously calibrated against radon from radium solutions furnished by the National Bureau of Standards. The standard deviation of repeated determinations of expired radon on single patients is estimated as ± 14 per cent.[41]

The nonexhaled radon was measured to an accuracy of about 10 per cent through its gamma-ray emission using a calibrated, thallium activated, sodium iodide, crystal scintillation counter.[23]

RESULTS AND DISCUSSION

The 19 patients who were still available of the original 32 injected by Schlundt, *et al.* were remeasured for radium content in May, 1951, and again in July, 1953. This was 235 months, and 261 months respectively, on an average, after the last injection received by the patients in 1931. The measurements were made in the Veterans Building of the Elgin State Hospital using the methods just mentioned. The results are presented in Table II along with the earlier data obtained by Schlundt *et al.*[37] For convenience of the reader the code letters referring to the patients have been retained exactly as in the original manuscript of 1933.

Most of the patients were cooperative

TABLE IV

MEASUREMENTS OF SMALL SAMPLES OF BONE FROM PATIENT 112 ILLUSTRATING NONUNIFORMITY OF RADIUM CONCENTRATION

Sample No.	Wet weight, gm.	Ra content μgm. $\times 10^{-4}$	Concentration, μgm. $\times 10^{-4}$/gm.	Sources of sample
5C2	.113	.124	1.1	Trabecular bone from head of humerus
9A6	.132	.198	1.5	Cortex of fibula
7C1	.087	.139	1.6	Cortical bone from tibia
8I3	.184	.369	2.0	Endosteal surface of femoral cortex
5C1	.124	.321	2.6	Cortical bone from proximal end of humerus
7L3	.151	.498	3.3	Trabecular bone from distal end of tibia
5C3	.075	.420	5.6	Superior segment of head of humerus
6R	.423	2.410	5.7	Parietal bone of skull
8D7	.131	.878	6.7	Trabecular bone from head of femur
9A8	.082	.779	9.5	Cortex of fibula
6Q	.407	3.948	9.7	Parietal bone of skull
8I2	.120	1.202	10.0	Cortex of right femur
8D6	.088	1.056	12.0	Cortical bone near head of femur

and free from apprehension during the collection of expired radon. With the exception of patient (O) who was combative, these people were generally unconcerned with the procedures and appeared to behave as well as or often better than normal patients. The error of the combined estimates, that is the error in the estimate of the total radium burden, probably does not exceed ± 20 per cent.

Since radium is contained almost quantitatively in the skeleton, these estimates of errors could be substantiated by measurements of bone specimens obtained from other cases of radium poisoning where *in vivo* measurements were made prior to surgery or autopsy. The fresh samples, sealed in glass tubes to prevent loss of radon, were measured in a pressurized gamma-ray ionization chamber. The concentration of radium per gram of fresh bone was multiplied by the estimated total skeletal weight (total skeletal weight was estimated as 10 per cent of the body weight[19]) to obtain the total radium burden. Although it is known that the radium concentration in bone is not uniform,[12,22] the use of large specimens of bone, as was ordinarily the case here, should give reasonably valid results. The data given in Table III show good agreement between radium burdens estimated from autopsy specimens and *in vivo* measurements. The lack of agreement between the results obtained from autopsy samples and the *in vivo* results reported by Aub *et al.*[2] in Patient 118 may be due to the fact that twelve years have elapsed since the *in vivo* determination.

Further evidence of the nonuniform distribution of radium in bone is given in Table IV which shows radium concentrations found, using the radon emanation method, in a number of small portions of bone taken from Patient 112 (M.K.). Areas of high and low concentration were selected using radioautographs of slabs of the bone[22] as a guide. The 10-fold range of concentration observed is substantially the same as that found by Dudley (see ref. 2) using densitometric measurements of radioautographs.

Norris and Evans[31] and Norris and Kisieleski[32] have shown that the retention and excretion of the alkaline earths, including radium, in rats and mice can be adequately represented as "power functions" (which plot as straight lines on log-log paper). Later, Hursh[14] demonstrated

that excretion of radium from the dog could also be described in this fashion. Unpublished data of the authors, obtained from 2 adult dogs injected with radium, corroborate this finding of Hursh and also supply information pertaining to the behavior of radium fractions contributing to exhaled radon and to retained radon as functions of time after injection. These data are presented graphically in Figure 2 in order to allow comparisons with the human data and to substantiate the applicability of the method of mathematical analysis. As will be brought out in more detail later, if the rate of excretion with time is a power function having a slope, b, then the rate of change of retention may be calculated as a power function with a slope, $b+1$. It will be noted that the retention measured in the one dog which was sacrificed (at 63 days) agrees with the prediction from excretion measurements.

The observed values of measurements of gamma-ray activity of these dogs have been corrected to an equilibrium value during the first thirty days after injection of de-emanated radium on the assumption that the state of the radium parent is such that the growth of Rn follows the theoretical pattern. The results demonstrate that the rate of decrease of the γ-emitting fraction as measured is far less than that of total retention. This convergence of the curves of total retention and the gamma-emitting fraction demonstrates that the expired radon fraction, which is the difference between the two, is decreasing with time.

Measurements of expired radon in general tended to exceed the prediction of the quantity of radium which contributes to this measurement. However, this was not surprising since the dogs hyperventilated themselves appreciably during the collection of the samples. Serial sampling of expired radon as a function of respiratory activity under anesthesia indicated that hyperventilation causes the quantity of Rn exhaled per minute to increase while the concentration of Rn per liter decreases.

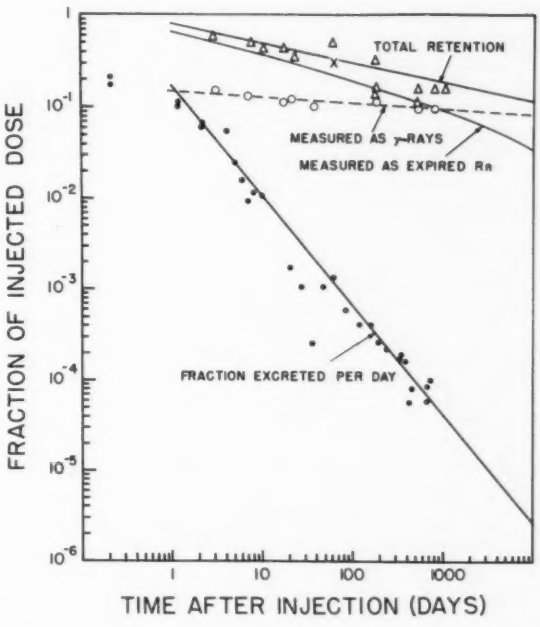

Fig. 2. Radium metabolism in intravenously injected dogs. ● = Measurements of total radium excreted per day $E_t = 0.17t^{-1.21}$. X = Total retention measured in sacrificed dog. The curve of total retention vs. time is derived from excretion data $R_t = 0.80t^{-.21}$.

Determinations of retained radium in the living animal:

1. ○ Measured as γ-rays.
2. △ Measured as expired Rn. The line drawn to represent the fraction appearing as expired Rn *vs.* time was derived as the difference between the curves of total retention and the γ-ray fraction.

Reductions in respiratory activity would presumably cause the opposite response.

Since the "power function" can be used to describe over-all radium metabolism in animals, an attempt was made to treat the data from humans in the same fashion. This treatment is presented with the realization that the function may have no particular significance insofar as the *precise* elucidation of metabolic behavior is concerned. Such might be better expressed as the sum of a large number of exponentials and, indeed, the data may be fitted by such a form. However, our inability to deal with the exponential form, both from the standpoint of lack of information and the computational difficulties encountered in

TABLE V

CONSTANTS OF THE RETENTION FUNCTION OF RADIUM IN HUMANS

Patient	No. of injections	Single dose approximation		Continuous injection approximation	
		A	b	A	b
A	15	.411	−.41	.411‡	−.41‡
B	15	2.254	−.73	2.183	−.74
C	15	.617	−.61	.617‡	−.61‡
I	18	.642	−.58	.715	−.58
J	20	.756	−.57	.676	−.57
O	26	.532	−.56	.434	−.59
P	25	.104	−.26	.078	−.23
T	11	.798	−.50	.523	−.46
Average	18	.577±23%*	−.53±.05†	.512±38%*	−.52±.055†

* Geometric mean and associated per cent error.
† Arithmetic mean and associated standard error.
‡ Further approximations did not give a better fit than already obtained using the constants from the single dose approximation.

empirically analyzing such a mathematical model, caused us to resort to the "power function" representation which describes well the available information, requires simple mathematical manipulations, and allows the estimation of sample statistics.

The method of injection to which the Elgin group was subjected differed somewhat from that used in the animal experiments. The Elgin patients received multiple equal dosages at weekly intervals whereas the animals were given single injections. However, the information derived from experimental animals allows the constants associated with the retention pattern in humans resulting from a single intravenous injection of radium to be determined, provided the following assumptions are made:

(1) Each dose is handled in like metabolic fashion.
(2) Neither a single dose nor any combination of doses has an effect on the metabolism of other doses.
(3) The retention function associated with each injection is independently described by the relationship:

$$R_t^* = Aqt^b \qquad b<0,\ t\geqq 1 \qquad (1)$$

where R_t^* is retention at t units of time after injection, q is the quantity injected, A is a constant which is equal to the fraction of q retained when t is equal to 1, and b is a negative constant.

Following these assumptions, if n repeated doses, q_i, are given at times t_i ($i=1, 2, 3, \cdots, n$) then the retention, R_t^*, at some time $t=t_n+\Delta t\geqq 1$ will be:

$$R_t^* = A\sum_{i=1}^{n} q_i(t-t_i)^b. \qquad (2)$$

When all values of q_i are equal to q, expression (2) simplifies to

$$R_t^* = Aq\sum_{i=1}^{n} (t-t_i)^b. \qquad (3)$$

Equation (3) gives the retention at any time $t=t_n+\Delta t\geqq 1$ after n equal doses injected at times t_i and describes exactly the retention of radium in the Elgin patients under the above assumptions. For purposes of comparison retention is usually expressed as a fraction, R_t, of the total injected dose. The equivalent expression is immediately obtained by dividing (3) by nq.

$$R_t = \frac{A}{n}\sum_{i=1}^{n} (t-t_i)^b \qquad (4)$$

However, because of the computational difficulties associated with expressions (2), (3), and (4), the estimation of the retention constants, A and b, by the use of these equations is impractical.

Graphic examination of the vehavior of Equation (4) demonstrates that after some period of time, depending upon the value of b, following the nth injection, the contribution from each equal injection to the total retention will be very nearly the same. Inspection of the data indicated that the most probable value of b lay between -0.6 and -0.4. Using these two values of b and with n equal to 18 (the average number of injections per patient) the behavior of R_t in Equation (4) with respect to time was determined graphically. This indicated that by 100 to 200 days after the last of eighteen consecutive weekly injections the fractional retention pattern is essentially that arising from the single injection of a quantity nq given at time $t=0$. Thereafter R_t may be closely approximated as

$$R_t' = At^b. \qquad (5)$$

Since the majority of Schlundt's measurements were made later than 100 days after the last injection, the "single dose approximation" (Eq. 5) was applied to the analysis of the multiple dose data, using the method of least squares on the log transforms of both R_t and t (in days) to estimate the constants (A and b) of the retention function. From the Elgin group, 8 patients were selected for whom three consistent ($t_3>t_2>t_1$, $R_{t_1}>R_{t_2}>R_{t_3}$) measurements of retention were available, and the individual retention constants determined (Table v). Figure 3 illustrates graphically the behavior of Equation (4) using the mean values obtained for these constants ($n=18$, $b=-0.53$ and $A=0.58$).

Where the interval between successive injections is small relative to the interval from the last injection to the time of measurement, the discrepancy between the retention measured following a series of discrete injections and the retention that would be measured if the same amount of material were administered at a uniform rate over the same period of time becomes negligibly small. Thus, the retention constants can also be estimated using the continuous injection model:

$$R_t''' = \frac{AC}{CT}\int_0^T (t-\tau)^b d\tau \qquad t \geqq T$$

$$= \frac{A}{T(b+1)}\left[t^{b+1}-(t-T)^{b+1}\right] \qquad (6)$$

Where A and b are constants of the retention function following a single injection, τ is the dummy integration variable with T being the total time of continuous injection (equivalent to the number of discrete injections times the interval between in-

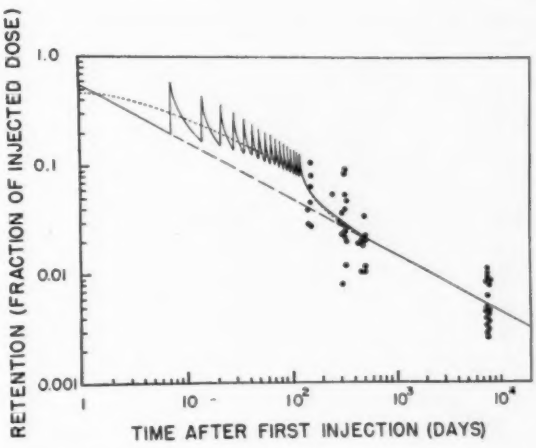

Fig. 3. Retention of radium in Elgin Hospital patients.

— — Single dose approximation $R_t' = 0.58t^{-.53}$

——— Summation of multiple injections

$$R_t'' = \frac{.58}{18}\sum_{i=1}^{18}[t-7(i-1)]^{-.53}$$

Eq. (4) using average constants estimated by the "single dose approximation."

– – – Continuous injection

$$R_t''' = \frac{.51}{18\times 7}\int_0^{18\times 7}(t-18\times 7)^{-.52}d\tau.$$

This continuous injection function is plotted with an adjustment in the time scale which places the times of the discrete injections at the means of the equivalent continuous injection periods.

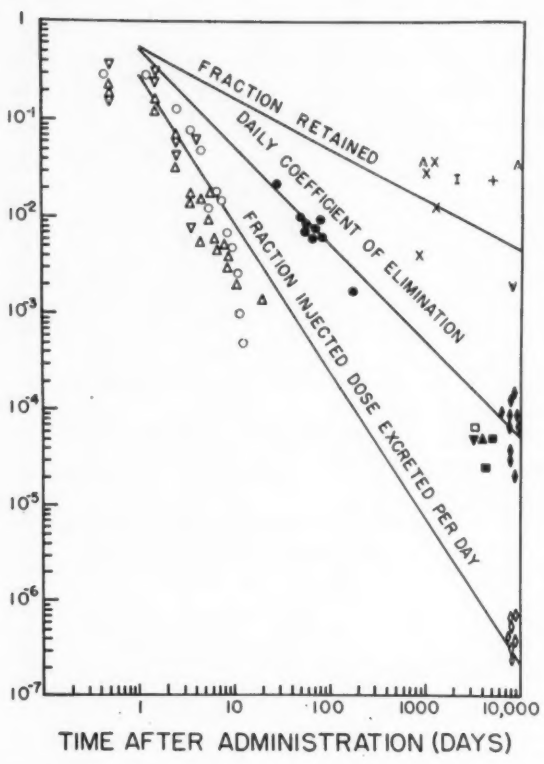

FIG. 4. The lines representing the coefficient of elimination (fraction of body burden excreted per day) and the fraction of the injected dose excreted per day are derived directly from the equation of retention (7). These plots are compared with existing data.

Retention (fraction of injected dose)

— Current study—average of Elgin patients: $R_t = 0.54t^{-.52}$

Λ Current study—early measurement refers to Case VII of Barker and Schlundt[3]

V Current study—Case III of Barker and Schlundt[3]

× Barker and Schlundt (oral and intravenous)[3]

\+ Stevens (intravenous)[42]

I Gettler and Norris (oral)[10]

Coefficient of elimination (fraction of body burden excreted per day)

♦ Current studies—all subjects

■ Schlundt and Failla (dial painters)[36]

▼ Aub, Evans, Gallagher and Tibbets (intravenous)[1]

▲ Aub, Evans, Gallagher and Tibbets (dial painter)[1]

● Aub, Evans, Gallagher and Tibbets ($RaCl_2$ inhalation)[1]

Values calculated following Evans' assumption of γ-ray representing 55 per cent of the total in the first and last instances. Intermediate points determined by subtracting measured excretion values from retention at period 1.

□ Craver and Schlundt[7]

Excretion (fraction of injected dose per day)

◇ Current studies—all subjects

△ Seil, Viol and Gordon (intravenous)[38]

▽ Seil, Viol and Gordon (oral)[38]

○ Rajewsky and Muth (inhalation $RaCl_2$)[33]

jections) in the same units as t, and $C = nq/T$ is the rate of injection. By a method of successive least squares approximations, constants A and b can be estimated. This model can be generally applied under the assumptions made above and will give unbiased results at all times over its interval of definition; whereas, the "single dose approximation" will include a bias unless the times at which retention measurements are made are several months removed from the time of the last injection. This method gives estimates of A and b that are in close agreement with those obtained using the "single dose approximation" method and in cases of repeated or continuous administration provides a more tractable mathematical system of calculation. The constants found using this approach are compared in Table V and in Figure 3 with those obtained by the alternative method. The compatibility between individual retention values and the empirically derived retention function using the continuous injection approximation was found, by Chi-square, to be exceptionally good ($0.80 < P < 0.90$).

It may be noted that the two functions are plotted in Figure 3 for eighteen weekly injections, which is the average number given the 8 patients, the data from whom are used in the previous mathematical analyses. The average number of injections for all the Elgin patients is 19.8 and since the curve is only slightly displaced by somewhat increasing or decreasing this number it is permissible to plot all the available retention data from the Elgin group on this graph using t_{18} as being equivalent to t_n for each patient. This is done (Fig. 3)

TABLE VI

RATE OF EXCRETION AND COEFFICIENT OF ELIMINATION OF RADIUM IN HUMANS

Patient	Date injected	Dose, μgm.	Date of measurement	Ra burden, μgm.	Excreta collection interval, days	Ra excreted per day, gm. $\times 10^{-12}$	Fraction injected dose excreted per day $\times 10^{-7}$	Fraction Ra burden excreted per day $\times 10^{-5}$	Per cent injected dose retained
Elgin Group A	1931	150	July, 1953	1.70	10.0	60.4	4.0	3.6	See Table II
Elgin Group J	1931	200	July, 1953	.93	9.8	132.0	6.6	14.2	
Elgin Group K	1931	200	July, 1953	.92	3.0	64.7	3.2	7.0	
Elgin Group N	1951	360	July, 1953	1.70	7.3	140.0	3.9	8.2	
Elgin Group S	1931	70	July, 1953	0.59	3.0	18.5	2.6	3.1	
Elgin Group U	1931	90	July, 1953	0.58	3.0	48.7	5.4	8.4	
101*	1927	250	Sept., 1951	0.50	—	—	—	—	0.20
103	ca. 1925	—	April, 1953	5.5	51.0	388.5	—	7.1	—
104†	1927	330	June, 1951	12.0	6.0	244.8	7.4	2.0	3.6
112	ca. 1925	—	Feb., 1948	1.1	11.0	175.8	—	16.0	—
116	1931	—	June, 1951	0.8	3.0	72.7	—	9.1	—

* Case III, Barker and Schlundt.[3]
† Case VII, Barker and Schlundt.[3]

using the time schedule originally published.[37]

The constants derived from the two methods of mathematical analysis are averaged to give a best estimate of the retention pattern of radium in humans as a function of time in days after a single intravenous injection.

$$R_t = 0.54t^{-.52} \qquad t > 1. \tag{7}$$

The use of the power function has the advantage that, given either the equation of retention vs. time or fraction injected dose excreted per day vs. time the other may be readily derived. In the instance of these data on humans, where the retention line has been derived experimentally, the equation of the line defining the fraction of the injected dose excreted per day as a function of time may be obtained by differentiating the equation of retention (5) which gives

$$\frac{dR_t}{dt} = bAt^{b-1} \tag{8}$$

or substituting the appropriate constants from Equation (7).

$$\frac{dR_t}{dt} = -0.28t^{-1.52} \qquad t > 1. \tag{9}$$

The retention and excretion functions are drawn in Figure 4 according to Equations (7) and (9) respectively along with previously published data for comparison.* Of particular interest are the actual excretion data from the Elgin patients (see Table VI) which are shown to be in good agreement with the prediction. Data from the analysis of excreta of patients other than the Elgin group have shown that no more than 3 per cent of the total radium excreted in long-standing cases is eliminated via the urine (see Table VII). This finding is substantially the same as that reported by Aub *et al.*[1] and by Rajewsky and Muth.[38] Therefore, only fecal specimens of the Elgin patients were analyzed.

TABLE VII

PARTITION OF EXCRETED RADIUM BETWEEN URINE AND FECES IN HUMANS

Patient	Collection interval, days	gm. Ra/day $\times 10^{-12}$			Per cent in feces
		Urine	Feces	Total	
103	51	5.5	383	388.5	98.6
104	6	3.8	241	244.8	98.4
112	11	3.8	172	175.8	97.8
116	3	1.7	71	72.7	97.7

* It should be noted that although Equation (9) is a daily rate equation, it cannot be used to calculate excretion in any one day at times close to the time of administration. This should be done by integration of (9), namely by using (7).

The coefficient of elimination (fraction of the total body radium excreted per day) may be calculated by dividing Equation (8) by Equation (5).

$$\frac{\frac{dR_t}{dt}}{R_t}=\frac{bAt^{b-1}}{At^b}=\frac{b}{t}=-0.52t^{-1}. \quad (10)$$

From the way this equation is derived, the slope of the corresponding line is always -1 regardless of the slope of the retention line, the only variation being in the intercept. This line is also drawn in Figure 4 and corresponding data derived from other workers are plotted for comparison. One will note that good agreement is also obtained in this case. The data of Aub *et al.*[1] obtained from a man who had inhaled a quantity of radium chloride also follow this pattern closely, indicating that inhalation of a soluble salt is followed by rapid solution and removal from the lung as opposed to the behavior noted by Marinelli *et al.*[24] following inhalation of insoluble radium sulfate.

If a person receives uniform daily injections or continuous administration of radium chloride over a period of time, the radium burden at any time t in days while treatment is continuing may be calculated. For this purpose Equation (7) is multiplied by its differential element, dt, and integrated from one to t. To this the fractional retention at the end of one day must be added and the entire function multiplied by the daily dosage, C, which gives

$$R_t=C[1.12(t^{.48}-1)+0.54] \quad t\geqq 1. \quad (11)$$

This function would be particularly useful if applicable to situations where the subject ingests an approximately constant amount of radium daily, as is the case with the naturally occurring radium content of food and water. Although it is ordinarily considered that the retention of orally administered radium is less than with intravenous injection, there is little or no direct information to substantiate this belief in the case of humans. On the contrary, it may be seen by reference to Figure 4 that data obtained following oral administration as well as the single case of inhalation of soluble radium salts follow the pattern found for intravenous administration. The work of Hursh and Gates,[16] Hursh[15] and Shandley[39] indicates that with an estimated daily radium dosage in food and water of 1.0×10^{-12} gm. a human retains 1.18×10^{-10} gm. Ra at the end of sixty-seven years. Substituting these values for C and for t in Equation (11) one obtains a value of 1.43×10^{-10} gm. Ra which is in surprisingly good agreement with Hursh's results when all the uncertainties are considered. Unfortunately, this is the only instance where both the daily radium dosage from natural sources and the radium content of comparable unexposed individuals is known. However, the agreement obtained in the above comparison suggests that such ingested radium is metabolized to the same extent as with intravenous injection.

From the preceding discussion it is apparent that any concept of a well defined "biologic half-time" of radium in bone is untenable. Schlundt, Nerancy and Morris,[37] and later Hoecker,[11] approximated constants for radium excretion in the Elgin patients on the assumption that the function was of the form of a single exponential. Hoecker also pointed out the possibilities of better describing the data with the power function. Aub *et al.*[2] have also attempted to describe radium retention in humans as a single exponential function. It seems evident that this technique will allow approximations only over limited periods of time.

If the equivalent Ra values represented by γ-ray activity and expired radon in the Elgin patients are viewed separately, it is noted that the rate of decrease of the γ-ray fraction with time is considerably less than that of either expired radon or total retention. This is qualitatively identical to the pattern described above in dogs. However, man appears to retain a smaller part of the injected dose in the γ-ray fraction and to lose it somewhat more rapidly. The data are plotted in Figure 5 and serve to further

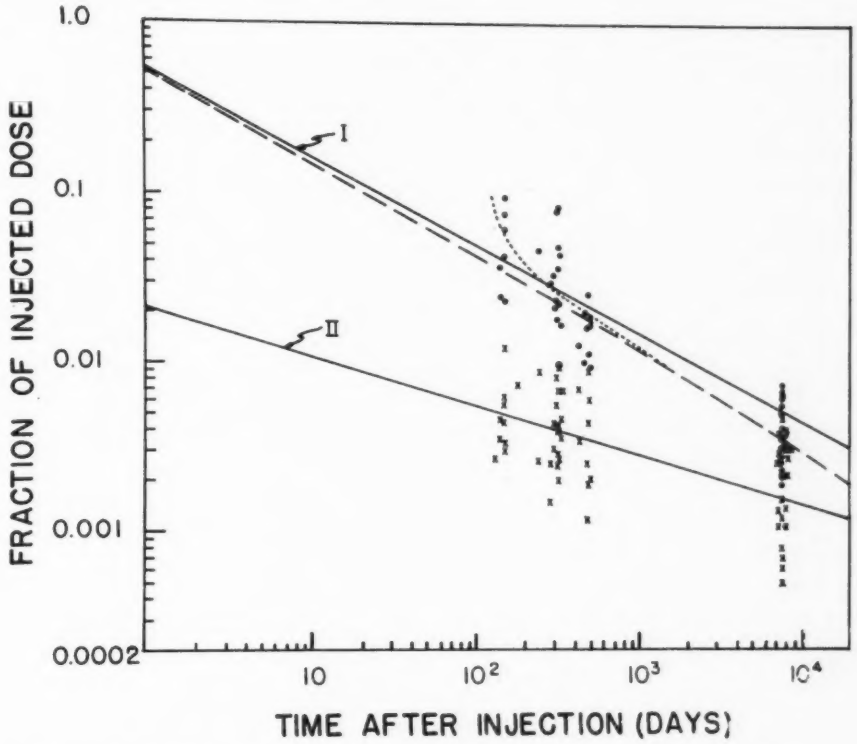

FIG. 5. Separate analysis of the fractions measured as expired Rn and as γ-rays in humans.
I—Total retention following a single intravenous dose of radium $R_t = 0.54t^{-.52}$
II—Fraction of single dose measured as γ-rays—individual measurements plotted as x, $\gamma_t = 0.021t^{-.28}$
— —Fraction of single dose measured as expired Rn (Curve I–Curve II)
- - - - - -Behavior of expired Rn fraction following the last of 18 injections of 10 μgm. Ra each at intervals of one week—individual measurements plotted as ●.

$$Rn_t = \frac{0.54}{60.48}[t^{.48} - (t - 126)^{.48}] - \frac{.021}{89.71}[t^{.712} - (t - 126)^{.712}]$$

illustrate the disporportionation of the two fractions as a function of time.

Since the γ-ray fraction in dogs was found to continue as a straight line function with time on the log-log plot while the expired Rn fraction did not, it is reasonable to assume that the same situation exists with respect to the human data. Therefore the equation of the γ-ray fraction has been derived using the "single dose approximation" method described earlier. Because of the small negative slope which exists in this case, the error in the measurements taken close to the last injection is small and the equation of the γ-ray fraction following a single intravenous injection is closely approximated as

$$\gamma_t = 0.021t^{-.28}. \qquad (12)$$

The fractional retention appearing as expired Rn after a single injection of radium, as indicated in Figure 5, is the difference between the single dose total retention and γ-ray functions

$$Rn_t = 0.54t^{-.52} - 0.021t^{-.28}. \qquad (13)$$

In order to best describe the results of measurements of the expired Rn fraction following multiple doses of radium in the Elgin patients the continuous injection approximation method has been used. Again the average number of injections (eighteen) has been used as n for all subjects. Using the continuous injection approximation, the fraction of the injected dose measured as expired radon may be calculated as

$$Rn_t = \frac{0.54\int_0^{18\times7}(t-\tau)^{-.52}d\tau - 0.021\int_0^{18\times7}(t-\tau)^{-.28}d\tau}{18\times7}. \qquad (14)$$

The behavior of this function with time after the end of the injection period is shown graphically in Figure 5 along with the actual measurements.

This continuing difference in behavior of these two fractions suggests that Ra may be metabolized in at least two distinctly different compartments at considerably different rates. It is of interest to speculate on the possible relationship between the more slowly metabolizing γ-ray component and the highly localized areas of high Ra concentration ("hot spots") which have been demonstrated in the bones of long-standing cases.[2,12,22] That the "hot spots" are mainly responsible for the γ-ray fraction is strongly suggested since they must also of necessity be metabolized at an extremely low rate or their identity would be lost. However, there exists no other evidence which relates to this hypothesis.

Inspection of Table II demonstrates that, in these long-standing cases of radium poisoning, an average of 70 per cent of the radon produced in the body is exhaled. All values necessary to these calculations were measured directly. This value of 70 per cent radon exhaled is considerably in excess of that of 45 per cent reported by Evans[9] and presently widely accepted as a basis for estimation of radium body burdens. Evans calculated total radon expired on the basis of an assumed respiratory minute volume and the radon content of 1 liter of expired air. It seems that Evans' use of an assumed breathing rate of 5 liters/min. for all patients[8] is largely responsible for this discrepancy. In the work reported here a total of 169 twenty minute breath collections were made from 19 men and 38 women under resting conditions. The resulting average value of 7.5 liters/min. is sufficient to account for the above difference in expired radon percentages. The wide deviation around the average of 7.5 l/min. (4.0 to 13.2 l/min.) encountered in measurements of minute volumes shows the inadvisability of using such an average value for accurate calculation of expired radon in individual cases.

The reported presence of MsTh, in many of Evans' early cases, may also have contributed to a lowered value for the fraction of radon expired. The short half-life (54.5 sec.) of thoron prevents its expiration to the same extent as radon and, in addition, there is more gamma radiation associated with 1 μc. of MsTh, than with 1μc. of Ra. The magnitude of these possible discrepancies has been discussed in detail by Evans.[2]

SUMMARY AND CONCLUSION

The concept of a well defined biological half-time of radium in bone is inconsistent with the long term data presented and an alternative is offered. Previously published information,[14,31,32] which shows that the retention and excretion of radium in animals may be represented as power functions, has been extended to the analysis of comparable studies in humans. The data presented are compatible with this form as are existing data in the literature. The use of the power function enables the derivation of the equation of retention from that of the excretion function or vice versa.

Where persons are exposed to soluble radium salts at a more or less constant level over an extended period of time, the application of the power function may be extended to predict radium burdens with time or to estimate the retention pattern following cessation of exposure.

There is substantial agreement among students of the subject that the presence of 0.1 μgm. of radium "fixed," that is, not being rapidly excreted, in the body has not been observed to be accompanied by deleterious effects, and therefore this quantity is currently defined as the permissible burden for man.[30] However, the relationship of radium burden to time has not been positively introduced as a factor. The data

presented indicate that the proper placement of the time of exposure in chronological time is of great importance in the prognosis of a given case. Since methods are available to determine both total radium burden and daily excretion of radium, it is now possible to use the daily coefficient of elimination as an index of elapsed time since exposure to a single equivalent dose of radium provided, of course, that soluble salts are known to have been involved and that allowance is made for the possibility of very recent exposures. Thus it is possible to estimate more certainly the course to be taken with regard to a specific individual.

The retention of intravenously injected radium in the human has been measured as 0.6 per cent of the original dose after twenty-two years. In this group of patients there was no noticeable effect of age or sex on the pattern observed; however, the group was largely composed of young, adult females and the numbers of males and old adults were so small as to make the observation inconclusive.

The behavior of the expired and retained radon fractions with time have been studied and described and the possible relationship of the retained radon fraction to "hot spots" is discussed.

The data include measurements of rate of radium excretion, concentrations in bone and comparisons of estimates of body radium burdens from *in vivo* determinations and from measurements of autopsy or biopsy specimens.

An average of 70 per cent of the total radon produced in long-standing cases of radium retention is exhaled.

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DOSAGE IN TANGENTIAL RADIATION THERAPY OF THE POSTOPERATIVE BREAST PORTAL

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INTRODUCTION

COMPLETE surgical extirpation is the treatment of choice for carcinoma of the breast, but sometimes this is manifestly impossible and even when the surgeon believes he has succeeded in removing all of the neoplasm, the histological examination of excised tissue may prove that he was mistaken. Radiation has been employed following surgery, and less frequently also before surgery, in an effort to salvage patients in whom the neoplasm has spread beyond the operative field.

Many methods of application of radiation have been used in the past, and review of this material has often revealed discouraging results.[2,12] These reports cover, in general, treatments given to low dosage levels (2,000 r or less tumor dose) and in some series the duration of treatment has extended six or nine months. Radiation of a more intensive nature has shown more encouraging results,[11,16] especially when the tumor dosage reaches 6,000 r.[1,9]

For these reasons, at our institution the low dosage approach formerly in use has been abandoned, and now postoperative breast carcinoma patients are treated with a dosage of between 5,500 r and 6,000 r as estimated or measured in potentially tumor bearing tissues. A time interval of eight to twelve weeks has been adopted. Wet epidermitis has been avoided, and to date (four year follow-up) few objectionable sequelae have been produced. If high dosage is required throughout all potentially tumor bearing tissues, careful evaluation of the evenness of distribution of the dosage is important.

The vascular supply and lymphatic drainage of the breast and chest wall are independent of that of the underlying lung. Because of this separation at the level of the pleura, irradiation of the lung adjacent to the involved breast is unnecessary. Because of the increased systemic effects from irradiation of large volumes of tissue, and because of the probability of radiation pneumonitis and fibrosis, irradiation of the lung is undesirable. As early as 1922, Finzi[5] suggested the use of glancing radiation to the chest wall to spare the underlying lung. The problems of dosimetry in tangentially treated fields have prompted the use of tissue density "bolus" material superimposed on the field so that estimations can be made of dosage using conventional isodose charts. The disadvantages of low dosage at the center of the treated area and even greater attenuation at the free edges of the field are inherent in this arrangement. Supplementary direct fields of radiation do not overcome these difficulties, but rather add new ones. Recent studies by Clarkson[4] and by Clarke[3] of dosimetry of the chest treated tangentially without bolus have encouraged us to consider use of this technique.

Considerable reliable information has been accumulated by our physics colleagues concerning the attenuation of radiation of varying qualities in water and other substances approaching tissue density. This information has been applied to clinical problems by the use of central axis depth dose tables and isodose charts. Measurements taken with chambers placed on the bodies of patients or within their body cavities have in our experience shown reasonable correlation with the charted dose when radiation was applied perpendicular to the patient's body surface. Less information is available concerning tangentially applied radiation and what there is pertains mostly to the application of isodose charts, usually

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of the central planes, to idealized chest wall curvatures. Little has been published on direct measurements of distribution of dosage over the entire treated surface or through the entire segment of the chest wall, and such information as is available suggests that there may be a variation of as much as plus or minus 50 per cent on the surface in the central plane and that the average dose may be considerably below that computed with isodose curves.[6] A comparative study of tangential irradiation was therefore planned, using techniques with and without bolus, and comparing them with the results of direct irradiation.

TECHNIQUE

Treatment commenced as soon after surgery as wound healing was complete. The patients received radiation to an anterior and a posterior portal arranged to crossfire the axillary, supraclavicular, and inferior cervical aggregation of lymphatic tissue. With the arm elevated, treatment was also given to an anterior thoracic field by means of two tangentially placed portals, one located at the contralateral sternal margin, the other adjacent to the posterior axillary line. The field was so arranged that a plane passing through the four corners of the field would measure 20 by 20 centimeters. This plane is convenient for reference. The curvature of the breast can be measured in terms of elevation above this plane. The tangential fields were arranged so that the central axis of irradiation was parallel to this plane.

In certain patients suspected of having metastases to internal mammary lymph nodes, it was desired to employ a sternal port in addition to the tangential port. To accomplish this the tangential portal was narrowed to a width of 15 cm. In 4 of the patients measurements were made of both 15 by 20 cm. and 20 by 20 cm. tangential fields. Technical factors used were 250 kv. (peak), half-value layer 1.4 mm. Cu, target-skin distance 50 cm. The output of the therapy unit was maintained at 72 r (measured in air) per minute. In addition, measurements were taken using a direct field of 20 by 20 cm. applied perpendicularly to the previously described reference plane. For the direct field, a half-value layer of 4 mm. Al, generated at 150 kv. (peak), was used, with target-skin distance of 50 cm. and output rate of 48 r (measured in air) per minute. Measurement of the 20 by 20 cm. fields of radiation produced by the machines at the 50 cm. target-skin distance indicated a coefficient of variation of the order of 7 per cent over the plane surface of a phantom.

MICROCHAMBERS

Small ionization chambers were selected as most satisfactory both in accuracy and speed of application. All measurements were made with type C Sievert-Rose condenser chambers.[14] The chambers measure 5 millimeters in diameter and 20 millimeters in length, and have a wall of electron metal and graphite and an air volume of 0.55 cubic millimeters. Electron metal is an alloy of about 90 per cent magnesium with a specific gravity of 1.85. An initial charge of 100 volts was used in all measurements.

The chambers were charged and measured with a Baldwin-Farmer type RB electrometer. One chamber was calibrated against a 100 r Victoreen graphite chamber which is maintained in the department as a secondary standard. Calibration was made on the surface and at various depths within a presdwood phantom with the qualities of radiation used clinically. The remaining chambers were compared with the calibrated chamber by exposure at the surface of a presdwood phantom which had been placed on a turntable. The chambers were placed equidistant from the center of rotation and 5 cm. from each other. The speed of the turntable was adjusted so that all of the chambers followed the same path through the field of radiation a minimum of six times during the exposure. In this manner, the chambers were checked against one another and against the Victoreen chamber periodically, and all remained within 2 per cent of the standard value. The output

of the roentgen-ray machines on periodic check has been maintained within 3 per cent.

The thoracic fields under treatment were divided into sixteen quadrilaterals, four rows of four each. A chamber was placed in the center of each quadrilateral. The positions of the chambers as well as the margins of the field were marked by tattooing the skin. Each chamber was held in place by a strip of adhesive cellophane tape, passing over the stem of the chamber. In most instances, the surface tissues were soft enough to allow pressing the chambers into the skin until they were half buried, an arrangement which approximates the actual surface dosage within 5 per cent.[4] Preliminary measurements failed to indicate any variation in chamber readings due to interference from adjacent chambers at the distance of separation used. The same chambers were used in the same position for each measured exposure.

SURFACE MEASUREMENTS OF PATIENTS

A special caliper having perpendicular sides and adjustable between 10 and 25 cm. is in use in the department.[10] When the caliper is placed with one foot on a medial and the other foot on a lateral corresponding corner of the field, the face of the applicator is readily brought into the correct position against the perpendicular side of the caliper so that the axes of the two tangential beams are coincident and parallel to the reference plane passing through the corners of the field.

Preliminary measurements were made on a group of 5 patients to determine the effect of two different types of applicators and the effect of differences in the size of the applied field. Using a light projection applicator by which a beam of light in register with the beam of radiation can be projected onto the area to be irradiated; beams 20 by 20 cm., 15 by 20 cm., 10 by 20 cm., and 6 by 20 cm. were measured without bolus. Radiation from a 15 by 20 cm. and a 20 by 20 cm. cone was similarly measured. No great difference was observed except for the 6 by 20 cm. beam. This beam had been chosen as being just wide enough to accommodate the greatest chest curvature commonly encountered in the postoperative patient. In the absence of bolus, the reduced dosage in this narrow beam cannot be explained as the result of diminished scatter at the patient, and scatter from distant parts of the room with larger fields is not sufficient to account for the difference. Inspection of the field pattern suggests that because of the narrowness of the field, the errors introduced in applying the beam to an actual clinical set-up are sufficiently great to place part of the breast in the penumbra. Because of this it is best not to employ fields smaller than 10 by 20 cm. Scatter from distant parts of the room with the 10 cm. width is not great. A radiopaque barrier placed not far from the margins of the field to limit the "wasted" portions of the tangential beam is permissible when bolus is used, but without bolus, the scatter which would come from such a barrier prohibits its use.

Table I

EFFECT OF VARIATION IN THE BEAM SIZE WITH AND WITHOUT BOLUS ON THE MEAN FIELD DOSAGE

	Beam Size in Centimeters			
	20×20	20×15	20×10	20×6
No bolus; cone	98.1 r	98.4 r	—	—
No bolus; light projector	98.4 r	99.1 r	98.1 r	87.5 r
Bolus; cone	—	80.4 r	76.2 r	66.3 r

Measurements were also made with various sizes of fields with bolus. As would be expected, considering the scatter from bolus, dosage is dependent upon field size. Results are summarized in Table 1.

During earlier measurements, considerable decrease in dosage was noted at the two medial corners of the field when the cone was used. This effect was more pro-

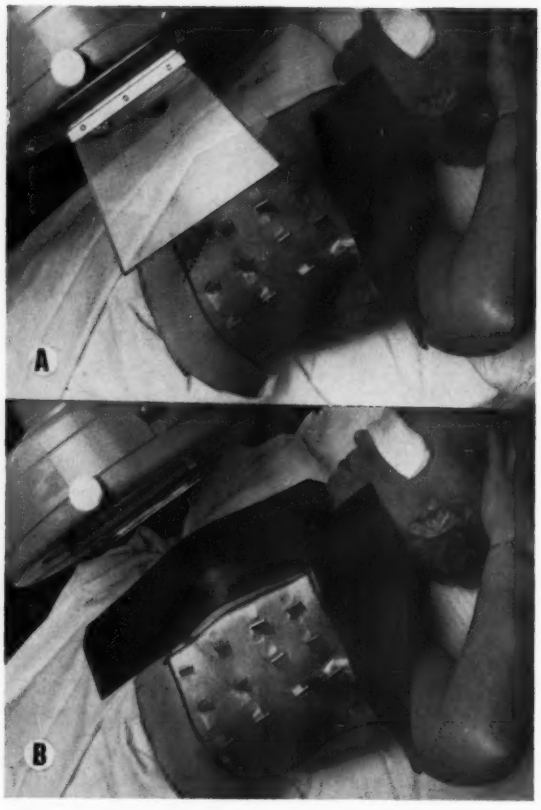

FIG. 1. (*A*) Cone, riding on apex of sternal curvature, projects a beam of radiation which curves to exclude the medial corners of tangential field. (*B*) When cone is omitted and beam lowered, the medial corners receive radiation. The curved lower edge of the projected beam is straightened by leaded mat on the skin. Further protective mats are used in actual treatment. Sievert-Rose chambers are shown in position.

nounced in some patients than in others. It had not been observed when the light projection applicator was used. Examination of the projected field of radiation readily provides an explanation. This is shown in Figure 1*A*. Here a lucite compression cone, substituting for the conventional cone applicator, has been attached to the light projection applicator. The light beam defines the radiation beam which, it can be seen, does not include the corners of the thoracic field. The corners of the cone are elevated because the straight edge of the cone must rest at the apex of the sagittal curvature of the sternum. In Figure 1*B*, the compression cone is omitted, the projected beam is lowered so that the corners of the field are included, and the edge of the projected beam is masked, so as to conform to the sternal margin of the field, by means of the leaded rubber mat placed just outside the sternal margin. A properly curved block, placed at the shutters of the light projection apparatus, could be used to adapt the beam to the curved sternal margin, but unlike the leaded mat, could not compensate for changes in elevation and curvature caused by respiratory movement. If treatment of the internal mammary lymphatic chain is to be accomplished, the omission of portions of the field adjacent to the sternum must be avoided.

Because of practical difficulties involved in deforming bolus material to conform to both the contours of the patient and the flat face of the roentgen-ray applicator, the use of a closed cone is mandatory, if bolus is to be used. A 15 by 20 cm. cone with a lucite closure of 4 mm. thickness was therefore used exclusively in the investigation. Care was taken to minimize the effect of sternal curvature described above. Because of both theoretical and observed variation in dosage attributable to variation from day to day in the packing together of the rice flour bolus bags on the patient, it was felt preferable to use a water bolus bag. A large chloroprene bag was enclosed in muslin and filled with 14 liters of tap water. The bag deformed readily to the smooth contours of the postmastectomy patients and provided a minimum of 14 cm. of scattering material above the thoracic wall. The bag was buttressed around the free edges with rice bolus bags and flattened against the face of the cone.

Seven patients referred consecutively for radiation therapy after radical mastectomy were subjected to measurement of the tangentially treated thoracic field. Five patients had left amputations; 2 had had the right breast removed. Only one measured exposure, consisting of equal doses from each of the two tangential directions, was given at any one treatment session. In random sequence, the patient received an aver-

Table II

COMPARISON OF TWO PATIENTS HAVING GREATLY DIFFERENT STERNAL AND INFRACLAVICULAR CURVATURES.

SUBJECT		20 X 20 FIELD, NO BOLUS					20 X 20 FIELD, BOLUS				
PATIENT HN.			−	−		++			−−	−−	
CURVATURES:	CM.	MEAN 97r			+		MEAN 71r	+			
STERNAL	1										
TRANSVERSE:											
INFRACLAVICULAR	1.5	C. OF VAR.	−		+		C. OF VAR.	+			++
MIDFIELD	4	12.1					14.9				
INFERIOR	5		−					+	−		
PATIENT HK.			−			+		−−	−	−−	−
CURVATURES:	CM.	MEAN 97r					MEAN 77r	+			+
STERNAL	2.5										
TRANSVERSE:											
INFRACLAVICULAR	3	C. OF VAR.					C. OF VAR.	+			++
MIDFIELD	4	10.1					17.4				
INFERIOR	5		−		+				−		++

FIELD DIAGRAMS ORIENTED TO LEFT THORAX. SEGMENTS WITHIN 10% OF MEAN, NO SYMBOL; BETWEEN 10% & 20%, + OR −, DEPENDING ON DIRECTION, BEYOND 20% DEVIATION FROM THE MEAN, DOUBLE SYMBOLS.

age of four measured exposures with glancing radiation to a 20 by 20 cm. field both with and without bolus, and to a 15 by 20 cm. field both with and without bolus. Two exposures each were give to a direct (perpendicular) 20 by 20 cm. field. The tangential fields received from each side at the cone surface 72 r measured in air (100 r with scatter). The direct fields received 62 r measured in air (100 r with scatter).

From the readings, the mean value for each chamber position from each method of irradiation was determined, and from these values the mean value for the field was derived. As an indication of the extent of variation or lack of "homogeneity" of the field, the standard deviation was computed and expressed as a percentage of the mean, or coefficient of variation. Standard deviation, σ, was computed from the formula:

$$\sigma = \sqrt{\frac{\Sigma_n (x_m - x)^2}{n}}$$

where x_m is the mean, x the position values, and n the number of positions.[16] Since the deviation from the actual mean was of interest rather than from a theoretical real mean, n and not n-1 was used as the divisor.

A chart of each field was constructed. To facilitate comparison all charts were arranged as for a left breast field, the left margin representing the sternal margin of the field, the upper portion the infraclavicular area. In each quadrilateral segment, the mean value of that position was placed, and the extent of deviation from the mean of the entire field was indicated by symbols when beyond 10 per cent. A single plus or minus, depending on the direction, was used to indicate deviation between 10 and 20 per cent. A double plus or minus was used if the deviation was above 20 per cent. The chest curvature was determined at the top, the center, and the bottom of the field in the transverse direction, and along the sternum in the long axis of each patient. The soft tissues remaining along the posterior axillary line could be deformed by the cone edge so that no curvature persisted. This scheme for measurement of curvatures was useful in indicating in a

TABLE III

A COMPARISON OF SURFACE MEASUREMENTS OF PATIENTS WITH SURFACE AND $D_{1.5}$ PHANTOM MEASUREMENTS

SUBJECT	20X20 FIELD, NO BOLUS	20X20 FIELD, BOLUS	20X15 FIELD, NO BOLUS	20X15 FIELD, BOLUS	20X20 DIRECT FIELD
PATIENTS D_0	− 82r 95r 98r 103r	72r − 62r 57r − 65r	− 81r 98r 91r 109r	72r − 72r − 62r 60r −	84r 93r 92r 86r
CURVATURES:					
STERNAL 1.5 CM.	93r 104r 107r 94r	++ 94r 75r 73r 77r	95r + 116r + 113r 98r	++ 102r 92 89r − 73r	91r 108r 102r 94r
TRANSVERSE:					
INFRACLAVICULAR 3 CM.	88r 103r + 107r 96r	++ 95r 79r 77r ++ 95r	93r + 117r + 112r 97r	++ 103r + 101r + 95r + 90r	91r + 104r + 105r 91r
MIDFIELD 4.5 CM.	− 82r 94r 101r 88r	80r − 68r 71r + 86r	− 86r 109 105r − 89r	85r 84r 87r 86r	86r 100r 101r − 78r
INFERIOR 5 CM.	MEAN 96r, C. OF VAR. 10.7	MEAN 77r, C. OF VAR. 16.9	MEAN 100r, C. OF VAR. 12	MEAN 85r, C. OF VAR. 19.4	MEAN 94r, C. OF VAR. 9.9
PHANTOM D_0	− 79r 89r 105r 91r	− − − − 73r 55r 50r 71r	− − 71r 103r 98r 96r	− − − − 50r 69r 69r 75r	90r 83r 89r 85r
CURVATURES:					
STERNAL 1 CM.	87r 96r + 110r 86r	++ 86r − 63r − 62r + 82r	− 86r + 110r + 111r 108r	+ 94r 85r 85r + 93r	94r 101r 100r 92r
TRANSVERSE:					
INFRACLAVICULAR 1.5 CM.	90r 91r + 111r 94r	++ 90r 67r 64r ++ 90r	− 84r + 113r + 112r 103r	+ 97r 91r 91r + 99r	91r + 105r 102r 94r
MIDFIELD 4 CM.	90r 102r + 109r 87r	++ 84r − 60r 66r + 80r	− 85r 106r + 111r 85r	89r 83r 85r 84r	88r 96r 96r 80r
INFERIOR 5 CM.	MEAN 95r, C. OF VAR. 9.9	MEAN 71r, C. OF VAR. 17.5	MEAN 99r, C. OF VAR. 12.5	MEAN 84r, C. OF VAR. 14.7	MEAN 94r, C. OF VAR. 6.7
PHANTOM $D_{1.5}$	− − 29r 27r − − 35r − 25r	− − − − 29r 45r 33r 28r	− − − − 13r 46r 40r 34r	− − − − 34r 41r 40r 26r	73r 74r − 67r − 67r
	++ 68r 79r + 66r − − 34r	++ 81r + 66r ++ 64r − − 40r	− − 40r ++ 77r ++ 76r − − 41r	− 45r ++ 71r ++ 83r − 44r	77r + 87r + 85r 73r
	− − 28r ++ 79r ++ 81r ++ 72r	− − 39r ++ 68r ++ 65r ++ 84r	− − 37r ++ 87r ++ 83r − 45r	− − 44r ++ 84r ++ 89r − 41r	74r + 90r + 89r 77r
	− − 23r ++ 80r ++ 83r 52r	− − 34r + 64r + 62r + 59r	− − 39r ++ 80r ++ 80r − − 33r	− 43r ++ 75r ++ 82r − 36r	70r 80r 81r − 62r
	MEAN 55r, C. OF VAR. 41	MEAN 54r, C. OF VAR. 33	MEAN 53r, C. OF VAR. 42	MEAN 55r, C. OF VAR. 38	MEAN 77r, C. OF VAR. 10

FIELD DIAGRAMS ORIENTED TO LEFT THORAX STERNUM AT LEFT, CLAVICLE ABOVE. SEGMENTS WITHIN 10% OF MEAN OF FIELD SHOWN WITH NO SYMBOL. SEGMENTS BETWEEN 10% AND 20% OF MEAN SHOWN BY − OR +, DEPENDING ON DIRECTION. SEGMENTS WITH MORE THAN 20% DEVIATION SHOWN WITH DOUBLE SYMBOL.

general way the character of the chest contours, but could not give complete information concerning topography. The results of the measurements of 20 by 20 cm. fields with and without bolus in 2 of the 7 patients are shown in Table II. These 2 patients exhibit the maximum and minimum sternal curvatures seen in the group. Patient HN also had the smallest curvature in the infraclavicular area of any of the patients.

SURFACE AND DEPTH MEASUREMENTS IN A PHANTOM

A phantom chest wall was constructed on a mold of the chest of patient HN. This patient was selected because she had the relative extremes of a minimum degree of curvature across one edge (upper) of the thoracic field and an ample curve across the other edge of the field. A series of tangential roentgenograms of 6 of the postoperative patients was examined and a thickness of 1.5 cm. was selected as a representative mean thickness of the postoperative chest wall. Measurements of necropsy specimens were consistent with this choice. A model thoracic wall was cast in Mix D, a tissue density wax.[8] The phantom wall was mounted in a phantom body segment constructed of presdwood and Mix D and containing a sponge lung which was adjusted to a density of 0.5 by the addition of water and then sealed in cellulose film. The specific gravity of the lung varies between 0.35 and 0.75.[13] The value 0.5 is reasonably representative and has been a commonly used value in dosimetry.[15] Measurements were made with the chambers half-buried in the surface of the phantom and at a depth of 1.5 cm., using the same techniques employed in the surface measurements of the patients. These results and the combined results of the patient's surface measurements are presented in Table III.

DISCUSSION

The consistency between readings of individual chambers and between mean values for the field for a single technique

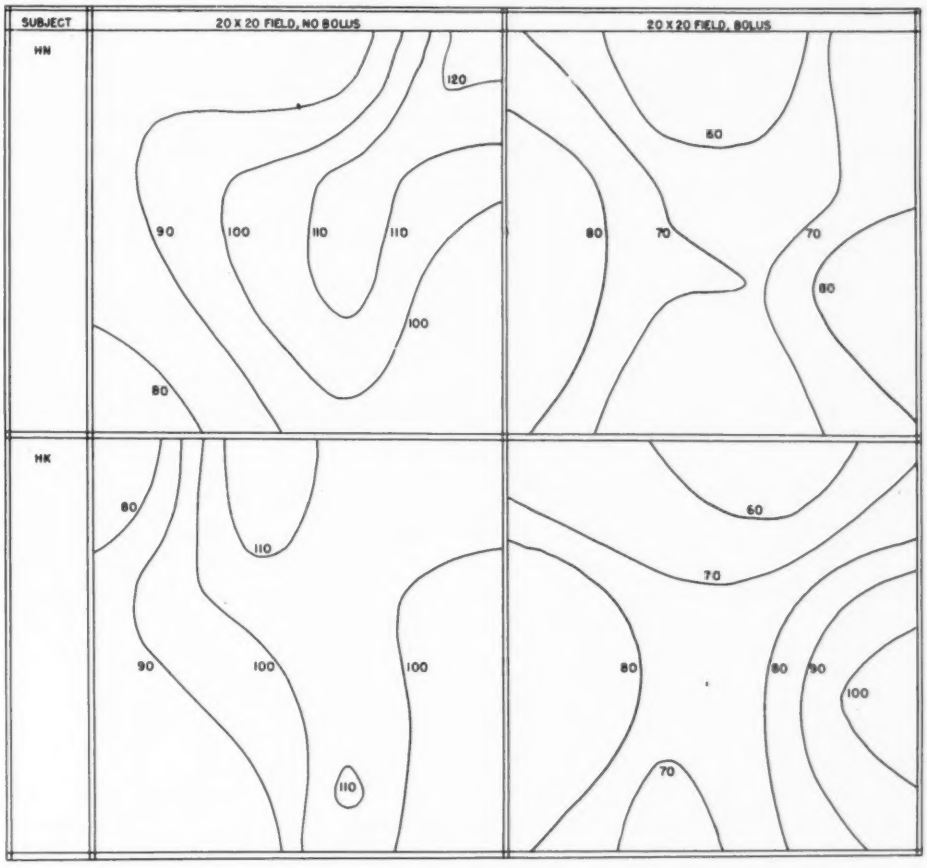

Fig. 2. Measurements of 20 by 20 cm. fields from Table II presented by the isodose curve method. Sternum is along left margin of each field and axilla is in upper right corner.

on a single patient were of the order of plus or minus 5 per cent of the mean of the respective group in most cases. Where this value was exceeded, the chambers affected were the corner chambers, usually those adjacent to the sternum. The placement of the cone is critical because of the effect of the curvature of the sternum. When the curvature is considerable, an appreciable portion of the field may be grossly underdosed. Bolus does not compensate for this effect as the scatter diminishes rapidly along the edges of the beam.

When the field is considered as a unit, variation in mean dosage of a single technique from patient to patient is not great and is within the range of experimental error. The differences obtained are too small to warrant any correlation with anatomical differences. Complex variations in surface contour tend to obscure relationships of dosage to curvature, although the effects of sternal curvature, of the point of maximum prominence in the transverse curvatures, and of the axillary depression are apparent. Dosage distribution is shown with and without bolus for a 20 by 20 cm. field for 2 typical patients in Figure 2 by the isodose line method. Plaster casts of the fields are shown to demonstrate the relationship of dosage to contour.

Certain features are common to all patients. The superior and inferior edges of the tangential field represent in each field the minimum and maximum curvatures, respectively. The minimal curve of the infraclavicular area is usually the area of minimal dosage, particularly when bolus is used. This is unfortunate because this area is the site of lymphatic channels which are

TABLE IV

COMPARISON OF DOSAGE AT THE CENTRAL AXIS (MIDFIELD) AS ESTIMATED FROM ISODOSE CHART AND AS MEASURED

Midfield Transverse Curvature	Subject	Field 20×20 cm. with Bolus				Field 20×15 cm. with Bolus			
		Medial	Medial central	Lateral central	Lateral	Medial	Medial central	Lateral central	Lateral
6 cm.	Isodose estimate	97	80	80	97	102	95	95	102
	PK	99	80	81	94	109	99	96	101
4.5 cm.	Isodose estimate	92	78	78	92	98	91	91	98
	PC	97	79	75	70*	—	—	—	—
	SM	98	81	79	82*	103	96	87	66*
	Mean Patient Values	95	77	75	86	103	97	91	85*
4 cm.	Isodose estimate	91	76	76	91	95	90	90	95
	HN	85	71	68*	80*	—	—	—	—
	HK	90	75	77	97	109*	100	97	90
	JN	97	80	73	94	90	90	89	81*
	Phantom D_0	88	74	74	88	96	88	88	96
3 cm.	Isodose estimate	88	74	74	88	94	87	87	94
	LS	96	75	73	76	—	—	—	—
Depth Dose	Isodose estimate	88	72	72	88	65	80	80	65
	Phantom $D_{1.5}$	60*	66	66	62*	45*	77	86	43*

* Deviation greater than 10 per cent.

part of the drainage of the breast,[13] and must receive adequate dosage.

A reasonable degree of correlation between measured dosage with bolus and isodose chart estimations can be obtained across the mid-transverse section of the fields. For each height of curvature, an arc was drawn to represent the mean curvature of those patients at this level. The distribution of chambers from sternum to posterior axillary line was marked off and the values at these points determined from a pair of charts for a 15 by 20 cm. short axis field.[7] This value for each of the patients and the phantom was compared with the corresponding values from the measured fields in Table IV. These measured values were derived as the means of the doses at the two adjacent chambers above and below the mid-transverse section. Correlation is found to be quite satisfactory and the values are within 10 per cent except toward the lateral margin of the field in certain patients. From examination of the field diagrams of these patients, the low values can be attributed to the negative curvatures of the axilla which lower the doses of the upper adjacent chambers. At the margins of the field, estimation of the dosage beneath the surface is made difficult because of the rapid change in dosage at the edge of the radiation beam. The $D_{1.5}$ values of the phantom suggest that the estimated values are likely to err in the direction of being too high.

Isodose charts are not generally available for planes at other than the central axes of the field. There is a tendency to determine dosage in the infraclavicular areas as well as elsewhere by extrapolation, but the practice should be discouraged, and even doses based on careful calculations by physicists must be applied cautiously. The infraclavicular area probably regularly receives less than the dosage estimated.

Evenness of dosage throughout the field appears to be slightly better in both the

narrow and wide fields when bolus is omitted. On the surface of patients, the homogeneity obtained without bolus approaches that of the direct field. There is an advantage when no bolus is used in that the greater dosage is centrally located. It may be fairly assumed that the probability of residual tumor is greater centrally, there having been a relative displacement of tissues toward the scar at the time of operation. Alternate treatments with and without bolus may be used and will improve the dosage characteristics between the center and the applicator edges of the field, but will not influence the low infraclavicular dosage.

At the $D_{1.5}$ level, representing the pleural surface and approximate level of the internal mammary lymph nodes, there is considerable spread of dosage for all glancing techniques, due principally to a rapid drop in dose at the sternal, infraclavicular, and axillary margins of the field. The dosage in the central portion of the field, when considered alone, is more satisfactory. When bolus is used, these central portions have received essentially the same dose as the surface. This is what would be predicted from isodose chart plots. In this respect, the bolus technique may be said to show a high degree of homogeneity. Without bolus, the central depth dose ($D_{1.5}$) in the phantom is about 75 per cent of the dosage of the overlying surface. The dosage in roentgens delivered to this level by a given incident dose is greater than with bolus. The more rapid attenuation of dosage as the depth increases when no bolus is used can be expected to better spare the lung.

The direct field has every advantage except that of sparing the lung. Lowering the half-value layer or shortening the target to skin distance will minimize but not eliminate this disadvantage. Electron beam therapy offers at high energy levels a theoretical advantage in the treatment of these postoperative portals because of the rapid drop in dosage beyond the level of maximum ionization, and we expect to explore this possible advantage in clinical material.

CONCLUSIONS

1. There is a slight improvement in evenness of dosage over the surface of tangentially treated breast portals when bolus is omitted. Tangential treatment without bolus gives more rapid attenuation of dosage from the overlying surface; with bolus the depth dose at the pleural surface in the center of the field is of the same order as the dosage on the surface, but represents a smaller percentage of the skin dose at the medial and lateral edges of the portal.

2. Reliance should not be placed on tangential radiation for treatment of the internal mammary lymphatics nor for treatment of the infraclavicular area.

3. General correlations between measurements and depth dose estimations from published charts can be readily made, but appreciable errors are possible, especially at the margins of the field, unless every detail of the patient's topography and the detailed relationships of the applicator to the patient's chest wall are taken into account.

4. Use of the light projection applicator, which is feasible when bolus is omitted, permits more accurate adaptation of the tangential beam of radiation to the contours of the thorax.

On the basis of these conclusions we have modified our technique and now use the light projection applicator for the tangential field and do not use bolus packing for this field. The infraclavicular area is included in the anterior and posterior fields cross-firing the upper lymphatic pathways. Bolus is, of course, used between the shoulder and the neck to compensate for the variations in thickness of the adjacent tissues. Greater use is made of the direct sternal portal for the treatment of the internal mammary lymphatic chain.

As no investigation was made of tangential radiation of the intact breast, no inference with regard to bolus in this application can be made.

The dosage from each of the two equal and opposing tangential applications is expressed as measured with backscatter (D_0) at the surface of the cone, or with the light applicator at the 50 cm. distance from the target. In our experience, with the factors and techniques used, this dosage has been shown to approximate the measured mean surface dose of the chest field within less than 10 per cent, and is used as the working dosage when prescribing the treatment without bolus.

SUMMARY

1. Low dosage postoperative irradiation of the breast is apparently without value, but dosages of the order of 6,000 r in tissue may be carcinocidal.

2. There is some question as to whether all suspected tissues receive such a dose with current techniques.

3. The dosage throughout tangential fields has been measured in a series of patients and in a phantom, the measurements being made both with and without bolus and compared with a direct field.

4. Fields without bolus showed slightly better surface homogeneity and produced greater dosage centrally, and the depth dose diminished rapidly from the surface.

5. Although tangential fields are desirable for treatment of the chest wall because they spare the lung, they cannot be relied upon for treatment of the infraclavicular tissues or the internal mammary lymph nodes.

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A BEAM DIRECTING CALIPER FOR TANGENTIAL RADIATION THERAPY

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MODERN radiation therapy calls for precise aiming of the beam of radiation. For the usual situation, where the axis of the cone of radiation is approximately perpendicular to the surface of the body, aiming is accomplished by such devices as back pointers, arc and pin assemblies, and protractors. Where the angle between radiation and body surface approaches 0 degrees in the so-called "glancing" or "tangential" techniques, no general purpose beam director is available, though Collins[2] and Allchin and Wilson[1] have published directors applicable to their particular techniques. The instrument presented here is applicable to any form of tangential therapy. It can be constructed easily at little cost and its clinical use is easily learned.

The instrument (Fig. 1) consists of fixed member *F*, a movable member *M*, a traveler *T*, a pointer *P*, and a wing nut. Both the fixed member *F* and the movable member *M* have a diagonal edge and a straight "working" edge, and the angular relationship between the two working edges is indicated by a protractor calibrated from plus 30 degrees through 0 degrees to minus 30 degrees. A setting on the plus scale indicates the entrance angle of radiation that is directed down onto the surface of the skin. At 0 degrees the two working edges are parallel and the beam of radiation is tangent to the surface of the skin. A setting on the minus scale indicates the entrance angle of radiation that is directed upward away from the surface so that only radiation which is from the edge of the

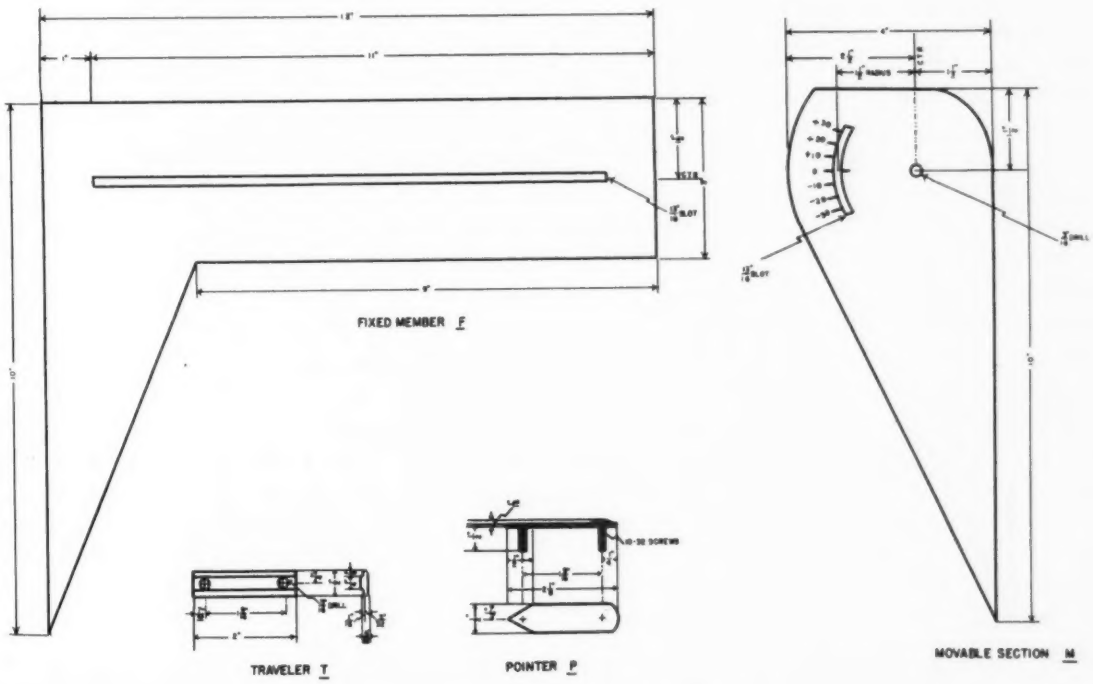

FIG. 1. Working drawing of caliper.

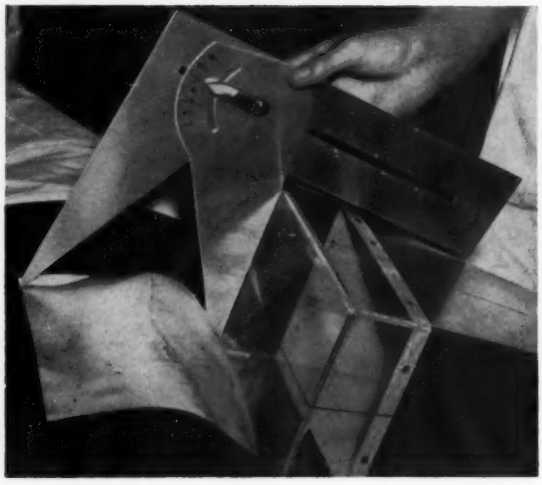

Fig. 2. Caliper viewed from front. Cone is being positioned for treatment of lateral side of the tangential field with radiation directed 10 degrees downward toward surface.

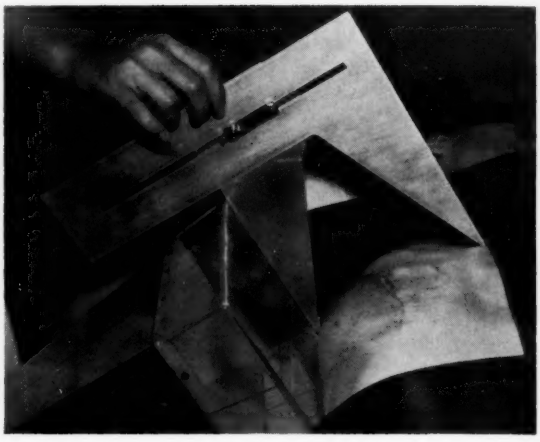

Fig. 3. Caliper viewed from rear. Cone is being positioned for treatment of the lateral side of the tangential field with the central axis of radiation parallel to the surface.

treatment beam and divergent to the central axis of radiation impinges upon the surface of the skin.

If, for example, it is desired to irradiate a 15 by 15 cm. area on the surface of the lower abdomen with the beam angled at 10 degrees downward and laterally, the caliper is employed as follows:

The tips of the two members are placed on the 0 and 15 cm. marks on a ruler and the *M* member is rotated until the protractor reads plus 10 degrees and locked in that position. After the caliper tips have been used to guide the marking of the treatment area, they are set on the two lateral boundaries of that area and then the roentgen tube is manipulated until the base of the cone is parallel with the working edge of *M* and in contact with it.

When the patient returns for another treatment, the caliper is set as it was before, thus providing a jig for aligning the beam of radiation at the desired angle relative to the surface of the skin.

In Figures 2 and 3, the caliper is shown in use in preparing the patient for radiation of a tangential breast field.

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CALCULATION OF DOSAGE IN VERTICAL ROTATION THERAPY USING STANDARD ISODOSE CHARTS*

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INTRODUCTION

ROTATION of the patient in the roentgen-ray beam is a useful technique in the treatment of certain types of deep-seated tumors. By this means, a definite volume of tissue can frequently be uniformly irradiated with a dose considerably greater than that received by other tissues, including the skin. Variations of the procedure include segmental scanning, and the combination of partial rotation with fixed ports.

It is desirable to determine dosage delivered at various points both inside and outside the continuously irradiated region. Various schemes have been devised for such calculations; because they are laborious they are frequently neglected, and only an estimate of the axis dose is recorded. A simplified procedure should be useful; the authors of this paper feel that they are here offering such a practicable method, which is at the same time more rapid and more accurate than others currently employed.

The system at present in use at the Presbyterian Hospital is based on one developed at the Massachusetts Institute of Technology for roentgen rays generated at 2 million volts. A discussion of its adaptation to 250 kv. has been published by Kligerman, Rosen and Quimby.[4] All calculations are referred to the "air dose at the center of rotation," and special charts have to be constructed for making the calculations. In developing and using these charts, it is assumed that the isodose curves are flat across the beam, that there is no beam divergence, and that depth dose changes only slowly with irradiated area. These assumptions are permissible in the supervoltage region, but they are not strictly justified in the conventional voltage range. It would be preferable to base calculations on standard isodose charts for the beams actually used. Such charts are employed in the method here presented.

STATEMENT OF THE PROBLEM

The problem is to determine the dose at a point in the interior or at the surface of an irregular contour, when the relative motion of the contour with respect to a beam of roentgen rays is one of rotation. The axis of rotation is parallel to the longitudinal axis of the patient, and both of these are perpendicular to the central axis of the beam of roentgen rays. The procedure for dose determination should be generally applicable, accurate, simple to use, and of minimal time consumption.

In rotation therapy there is a region within the contour which is continuously irradiated. Points outside this region receive radiation only during that part of the rotation when they are within the beam; the dose received by such points will depend on the ratio of time spent within the beam to the total time of revolution, and on the average thickness of tissue traversed by the radiation in reaching the point in question.

Let the cross-section of the body at the level of the tumor be indicated by the oval outline in Figure 1. The inner circle represents a spherical, centrally located tumor. The body is to rotate about an axis through the center of this tumor. For diagrammatic representation at this time it will be assumed that the patient remains fixed and that the target revolves about the axis at a distance *FAD*, so that its path is indicated by the outer circle. All geometric

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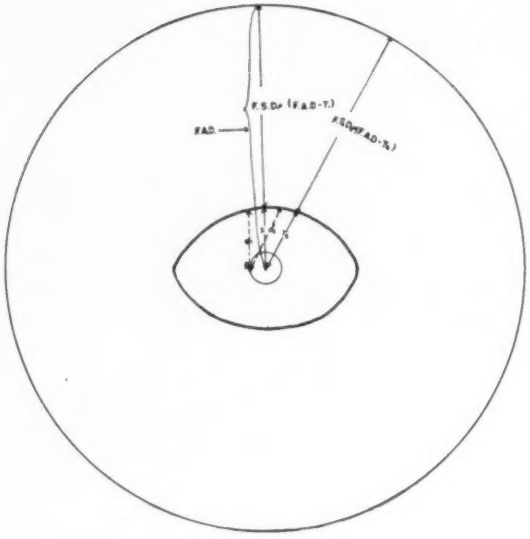


FIG. 1

relations remain the same as if the patient rotated and the target was stationary.

P represents a point on the periphery of the tumor. In actual rotation it would traverse a circular path. Under the present simplification it remains fixed and the target moves. The instantaneous percentage depth dose delivered to this point, for a particular quality of radiation and beam size, is determined by the instantaneous focal-skin distance *FSD*, and the tissue depth *d*. Since the body contour is not circular, but roughly elliptical, as the patient rotates the focal-skin distance and the tissue depth vary continually. The focal-skin distance for any position can be found by subtracting from the target-axis distance the semi-diameter of the body along the particular axis. ($FSD_2 = FAD - T_2$, etc.) The tissue depth *d* for each position must be measured along a line parallel to the corresponding *T*, as indicated. For the point at the axis of rotation $d = T$, but for all other points these differ constantly. Furthermore, unless the point is at the axis of rotation it will lie on the central axis of the roentgen-ray beam for only two instants, for most of the time it will travel through regions on one side or the other of this. Therefore the actual dose delivered to the point will be less than the value obtained by averaging central axis depth dose values only. This difference is small for high kilovoltages, when isodose contours are relatively flat, but may be considerable for lower kilovoltages or small fields, where isodose curves vary rapidly near the divegent edges of the beam.

METHOD OF DOSAGE CALCULATION

By dividing the patient's contour into a large number of segments and considering the rotation as a series of stationary fields over these segments, an approximation of the dose delivered at any point can be made. As just stated, focal-skin distance, tissue depth, and position of point within the field will change from one position to the next. However, a simple graphical approach facilitates calculating the partial doses and then summing them to get the total dose.

In the paragraphs that follow, successive stages of approximation to dosage determination are outlined. In Figure 2, the central part of Figure 1 is enlarged, to show a transverse contour of the patient, with the outline of the tumor drawn inside. The axis of rotation is to pass through the center of the tumor.

It is convenient either to draw radii out from the axis of rotation at every 10 degrees, or to work with the chart superimposed on polar coordinate paper. The contour is divided into 12 segments each consisting of 30 degrees, as indicated. Segment

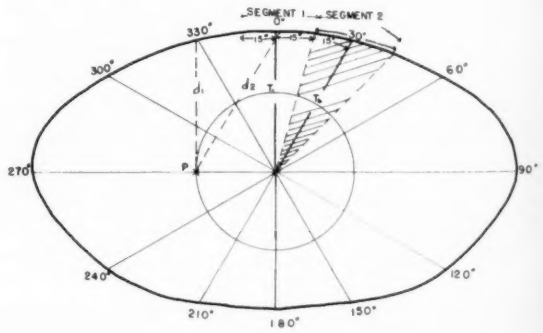


FIG. 2

Table I

1	2	3	4	5	6	7
Segment	Tissue traversed, cm. (T_n)	Focal-skin distance, cm. $=85-T_n$ (FSD_n)	Air dose, r/minute $=\frac{20.7\ (85)^2}{(FSD_n)^2}$ (AD_n)	Tissue depth, cm. (d_n)	Per cent depth dose at d cm. (by interpolation from standard tables) (% DD_n)	Instantaneous roentgens $=\%DD_n \times AD_n$ (R_n)
1	9.25	75.75	26.10	8.40	56.40	14.70
2	9.80	75.20	26.40	10.20	44.50	11.70
3	12.50	72.50	28.40	15.20	26.30	7.50
4	15.50	69.50	30.90	20.20	11.00	3.40
5	12.60	72.40	28.50	15.50	23.80	6.80
6	10.60	74.40	27.00	10.60	42.00	11.30
7	9.25	75.75	26.10	8.30	56.40	14.70
8	10.50	74.50	26.90	8.50	56.00	15.10
9	12.70	72.30	28.60	9.30	50.70	14.50
10	15.50	69.50	30.90	10.70	42.50	13.10
11	12.70	72.30	28.60	9.30	50.70	14.50
12	9.80	75.20	26.40	8.30	56.70	15.00
Average						11.80

1 extends 15 degrees on either side of the zero degree radius, segment 2 extends 15 degrees on either side of the 30 degree radius, etc.

Consider the point P on the periphery of the tumor, as in Figure 1. As the axis of segment 1 lies on the axis of the beam, the applicable target-skin distance is $FAD-T_1$, the tissue depth d_1. Now as the body rotates to bring the axis of segment 2 onto the axis of the beam, the target-skin distance is $FAD-T_2$, and the tissue depth is d_2, measured along a line parallel to the axis. Similar values can be obtained for all segments. At each position an approximation of dosage is to be made.

In order to use standard dosage tables or charts, it is necessary to have some constant point of reference. For fixed fields, doses are stated in terms of roentgens at the skin, or roentgens in air at the distance of the skin. In rotation, since this distance is variable, the dose rate at the skin does not remain constant, and the percentages cannot be immediately applied to a known value. However, a convenient reference constant is the roentgens per minute in air at the distance of the axis of rotation. If this number is denoted by K, then the instantaneous roentgens per minute in air at the position of the skin, when the axis of any particular segment coincides with the axis of the beam, is found by application of the inverse square law to be

$$K\times\frac{(FAD)^2}{(FSD_n)^2}=K\times\frac{(FAD)^2}{(FAD-T_n)^2}.$$

The successive approximations to be discussed are most readily explained by reference to a particular case. The contour is shown in Figure 3, with a central lesion 10 cm. in diameter, located in an abdomen 31 cm. by 18.5 cm. The lesion is to be treated with 250 kv. roentgen rays, half-value layer 1.5 mm. Cu, target-axis distance 85 cm., field 10×10 cm. K, the roentgens per minute in air at the position of the axis, is 20.7.* The point under consideration, P, lies near the periphery of the lesion, as indicated.

* This value, rather than a round number, was chosen because it was the actual output used in the experimental checks described later in the paper.

TABLE II

ROENTGENS AT DEPTH PER 100 ROENTGENS IN AIR; AREA 100 SQUARE CM.

H.V.L. (mm. Cu)	1.0			1.5			2.0		
F.S.D.	70	72.5	75	70	72.5	75	70	72.5	75
Depth									
0	136.0	136.0	136.0	131.0	131.0	131.0	126.0	126.0	126.0
3	112.0	112.2	112.5	107.5	108.1	108.7	103.0	103.5	104.0
5	87.0	87.2	87.5	85.0	85.3	85.7	83.0	83.2	83.5
7	67.0	67.2	67.5	66.5	66.8	67.2	66.0	66.2	66.5
10	45.0	45.2	45.5	46.0	46.3	46.7	47.0	47.2	47.5
15	24.0	24.5	25.0	25.5	26.0	26.5	27.0	27.2	27.5
20	11.0	11.0	11.0	12.0	12.2	12.5	13.0	13.2	13.5

A table is constructed to show 12 semidiameters (T_n), 12 focal-skin distances (FSD_n), and 12 corresponding air doses at the different distances (AD_n), as indicated in Table I, columns 2, 3, and 4. Also 12 tissue depths (d_n) are measured and entered in column 5. Using these factors, it is possible to interpolate between focal-skin distances in standard depth dose tables to obtain a definite per cent depth dose corresponding to any particular values of FSD_n and d_n (column 6). Once the per cent depth dose corresponding to any pair of values is found, the instantaneous roentgens per minute to the point P are found by multiplying this per cent depth dose by the instantaneous air dose rate given in column 4. These products, entered in column 7, are averaged to give the average dose rate at the point during a period of one rotation.

This is the *first approximation*. The results of this calculation should be the same as those obtained from the special curves calculated according to the method used at present.[4] Because of the extensive and tedious interpolation in the depth dose tables, it does not offer any real advantage over that method. If this difficulty could be overcome, the major deterrent toward the development of a simpler scheme would be resolved. Consideration of the effects of slight shifts in focal-skin distances shows that this is practicable.

For any contour the *FSD* will vary between some maximum and some minimum. For example, in the case under discussion the maximum is 75.75 cm, and the minimum is 69.50 cm. The average value is 73.3 cm. In Table II are listed depth doses determined from standard tables[1] for an area of 100 square centimeters, half-value layers 1 mm. Cu, 1.5 mm. Cu, and 2 mm. Cu for *FSD*s of 70 cm., 72.5 cm., and 75 cm.

It is seen that the depth doses for these three focal-skin distances never vary by more than 1 per cent of the air dose, for the qualities of radiation indicated. This fact permits the use of a single focal-skin distance, rather than twelve, with the assurance that any instantaneous error due to this simplification will never exceed plus or minus 1 per cent, while the total error, averaged over the twelve segments, should be smaller. Thus the inconvenient interpolation can be avoided by the use of a single average focal-skin distance. A next step makes it possible to adopt only a very few average distances as suitable to cover all cases.

In practical treatment, a wide variety of contour sizes and of tumor sites must be considered. These will include central, moderately eccentric, and extremely eccentric lesions. Head dimensions are approximately 15 by 20 cm.; the normal abdomen is about 20 by 30 cm.; while stout people may be 30 by 40 cm. For these variations in size, and an 85 cm. *FAD*, the

maximum *FSD*s are 77.5, 75, and 70 cm. respectively; the minimum *FSD*s are 75, 70, and 65 cm.; the averages are 76.3, 72.5, and 67.5 cm. These variations notwithstanding, it is possible for normal and stout people with centralized abdominal lesions to use a single *FSD* of 70 cm. without significant error, while for heads an *FSD* of 80 cm. is satisfactory. For eccentric lesions the variations in *FSD* are somewhat greater, but in general they are still insufficient to cause considerable error, although possibly for a very eccentric lesion in a chest this ought to be checked.

Applying this approximation to Table 1, columns 1, 2, 4, and 5 remain unchanged; column 3 is *FSD* 70 cm. throughout, column 6 becomes Per Cent Depth Dose at *d* cm. These values are now read directly from standard depth dose tables for 70 cm. target-skin distance, for the field and quality specified above. Values in column 7 are obtained as before, by multiplying each per cent depth dose by its corresponding air dose.

When these changes are made in this particular case the average of the values in this column remains 11.8 as it was before. It will seldom change by an appreciable amount. This is the *second* approximation method; it is evident that values are close to those of the first method, and the calculations are greatly simplified. As a further simplification, a single average air dose (*AD*), the average of all the values in column 4, may be used instead of the 12 different ones. In this case the average instantaneous dose is obtained by taking the average of the per cent depth doses as above, and multiplying this by the average air dose. It eliminates column 7 of the previous tables. For the example under consideration the dose obtained in this manner is again 11.8. This is the *third* approximation and the simplest of all. For this particular case it does not differ from the more accurate first method. For many dosage problems this procedure is adequate, especially in cases with centrally located lesions.

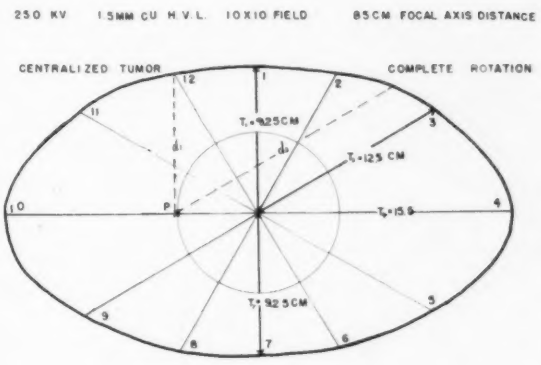


Fig. 3

The major error in these approximations comes from the use of axis depth dose values. As was shown previously, unless the point in question is at the axis of rotation, it is actually subject to central axis doses at two instants only, and lies on either side of this central ray for the remainder of its circular route. Therefore the actual dose will in general be somewhat less than that calculated as above. The error, small for high kilovoltage radiation with its flat isodose curves, may be significant in the 250 kilovoltage region.

It is a simple additional step to adapt the procedure just outlined to the use of isodose charts instead of tabulated values. Standard isodose charts are employed; they are traced on fairly stiff celluloid, and made with a slit along the center line. A pin passed through this slit can be inserted into the center of rotation of the contour diagram, and the chart slid back and forth so that its surface line can always be made to coincide with the surface of the contour. A large celluloid sheet with polar coordinates as in Figure 2 will facilitate operations. The contour (Fig. 3) is placed over this celluloid sheet, with the center of the tumor directly over the center of the polar coordinates.

The specially constructed celluloid isodose chart is placed directly above the contour, with the pin passing through the slit and inserted at the center of rotation. For this particular problem the chart is for 70 cm. *FSD*, with a field of 10 by 10 cm., to

cover the tumor* (Fig. 4).

With the center line of the isodose chart superimposed on radius 1 (Fig. 4*A*) and its surface coinciding with the surface of the contour, the tissue thickness T_1 is read from the center of the tumor to the surface of the contour. At the same time the percentage depth dose at point P is noted ($\%DD_1$).

Then the center line of the isodose chart is moved to radius 11 (Fig. 4*B*), tissue thickness T_2, and the instantaneous per cent depth dose $\%DD_2$ is determined. The same procedure is carried out for the twelve segments.

It must be pointed out that in taking these readings the following procedure is to be used. The quantities T_1, T_2, etc., are read with the isodose chart surface, *AB*, crossing the point of intersection of the axis *CD* and the outer contour of the patient, as indicated at P_1 (Fig. 4*B*). The quantities DD_1, DD_2, etc., are read with the isodose chart moved along the slit so that the line *AB* touches the contour at the point of intersection of the line *EF* passing through the point itself, as indicated at P_2 (Fig. 4*C*). In this manner, (*B*) gives *T* for the best average air dose for the segment, while (*C*) gives the best average per cent depth dose.

A table is constructed in the same form as Table 1, but the values are now taken from the isodose charts. For the point in question the data are shown in Table 111. Again the average dose received during a complete revolution is the average of the values in the last column. This is the *fourth* approximation, and should give the most nearly correct value.

The differences between corresponding values in column 7 of Table 111 and column 7 of Table 1 indicate the effect of using isodose charts instead of center line values. The result, 10.4, is 12 per cent less than the 11.8 obtained from axis doses only. It should be noted that the point under investigation is on the periphery of the tumor, and, therefore, during part of the rotation, will be almost at the edge of the isodose chart, where variations from center line doses are greatest. For points nearer the center of rotation, differences between results obtained by this method and by use of center line values will be smaller.

In this case, as with the use of center line values, it is possible to use a single average air dose (average of values in column 4) which is to be multiplied by the average of the values in column 6. In the case under consideration the final result is 10.5. This is the *fifth* approximation. For central lesions its result differs little from that of the fourth, but for eccentric ones it is usually desirable to use the 12 partial values.

This is the procedure for one point. In actual practice, for each setting on a particular numbered radius, readings can be taken for all points at which the dosage is to be determined.

A division of the circle into twelve parts was found to be adequate in all cases studied. The greater the number of divisions, the greater will be the accuracy of the final average.

For a point not continuously in the beam (*e.g.*, a point on the skin), it is necessary to multiply the value for the segments in which it enters and leaves the beam by a proportionality factor $R/30$, where R is the number of degrees during which the point is in the beam for that particular segment. The readings for percentage depth dose (*DD*) in these segments should be taken with the center line of the isodose curve coinciding with the center line of this subsegment.

Instead of working out the inverse square law calculations to obtain the different air doses corresponding to the various focal-skin distances, it is practicable to construct a chart for finding the factor by

* The surface area irradiated is not constant, but varies because of the varying diameters of the body, and consequent variations in *FSD*. Any error due to this can be considerably reduced by properly setting the collimating diaphragm. For any one setting of the diaphragm the area irradiated will be larger or smaller depending on whether the skin is farther away or closer to the target. An average setting is achieved by first setting the diaphragm to give the required area at the closest skin position, then resetting for the farthest, and finally using an intermediate setting.

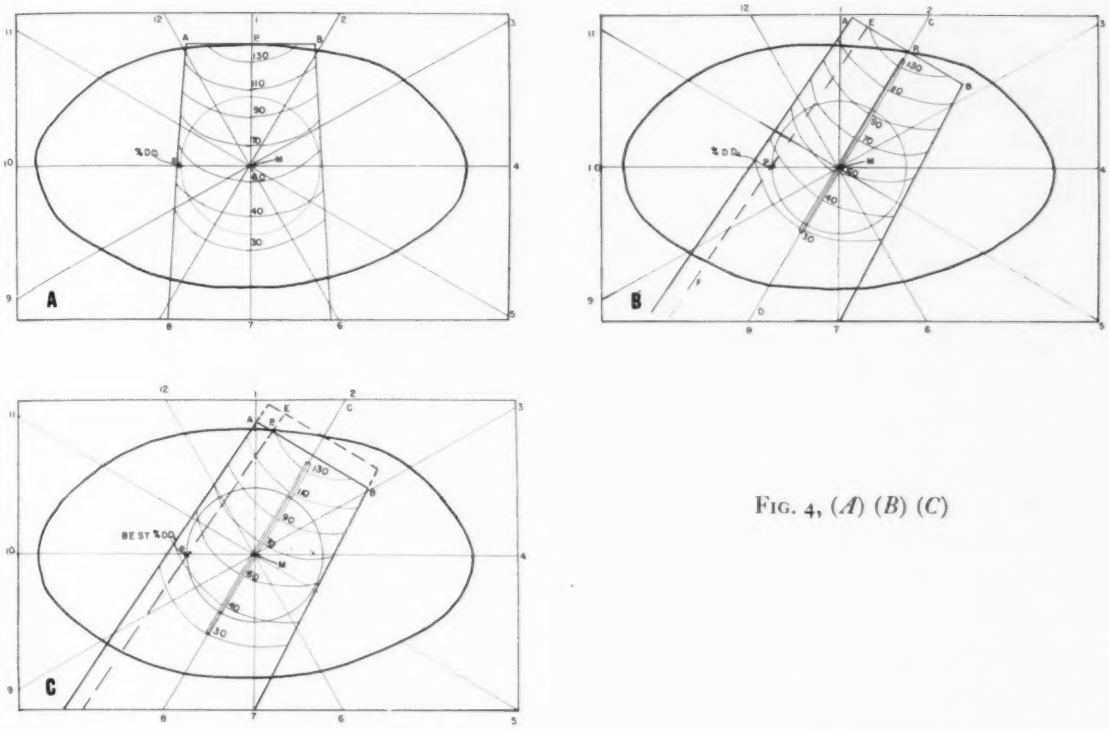


FIG. 4, (*A*) (*B*) (*C*)

which K (air dose at 85 cm.) must be multiplied for each T. Such a chart is given in Figure 5. Thus for a tissue depth of 10 cm., the air dose at the position of the skin would be 1.28 K.

In order to test the validity of the dosage calculations just described, two simulated cases were treated by means of a pressdwood phantom shaped like a human thorax. Doses were calculated for various points in

TABLE III

1	2	3	4	5	6	7
Segment	Tissue traversed, cm. (T)	Focal-skin distance (FSD)	Air dose, r/minute $=\frac{20.7\ (85)^2}{(FSD)^2\ (AD)}$	Tissue depth, cm. (d_n)	Per cent depth dose at d cm. from standard tables (% DD)	Instantaneous roentgens $=\frac{\%\ DD \times AD}{R}$
1	9.25	70	26.10	8.40	43	11.2
2	9.80	70	26.40	10.20	37	9.8
3	12.50	70	28.40	15.20	25	7.1
4	15.50	70	30.90	20.20	11	3.4
5	12.60	70	28.50	15.50	22	6.3
6	10.60	70	27.00	10.60	36	9.7
7	9.25	70	26.10	8.30	43	11.2
8	10.50	70	26.90	8.50	45.5	12.2
9	12.70	70	28.60	9.30	48	13.7
10	15.50	70	30.90	10.70	43	13.3
11	12.70	70	28.60	9.30	48	13.7
12	9.80	70	26.40	8.30	49	12.9
Average						10.4

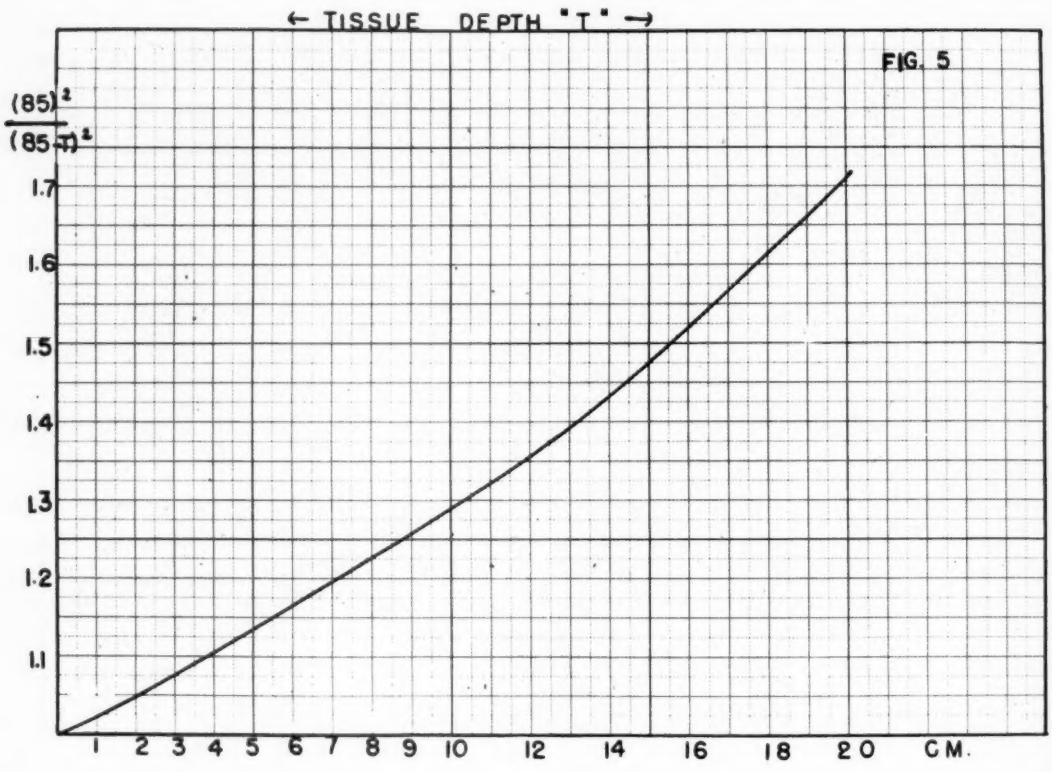


FIG. 5

a centrally located and an eccentrically located tumor (Fig. 6*A* and *B*), and were measured for the same points by means of a Victoreen ionization chamber placed in a cavity at the point in question. Four variants of the calculation scheme were employed:

1. As described above, using isodose contours and 12 different average depths.

2. Using isodose contours and a single average depth, which is the average of the 12 averages of method 1.

3. Using "flat isodoses" (central axis values only) and 12 average depths.

4. Using central axis values and a single average depth. In addition, calculations were made from charts developed according to the Massachusetts Institute of Technol-

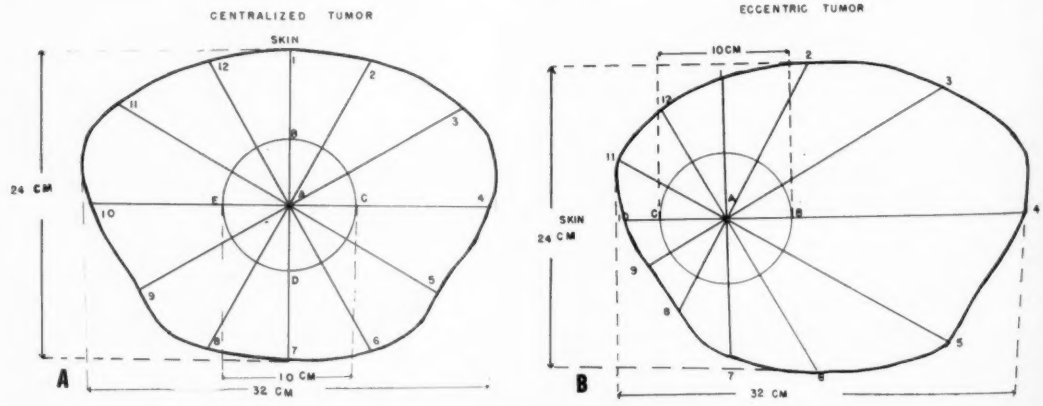


FIG. 6 (*A*) (*B*)

TABLE IV

CASES TREATED BY MEANS OF A PRESSDWOOD PHANTOM SHAPED LIKE A HUMAN THORAX: 250 KILOVOLTS; 1.5 MM. Cu H.V.L.; 10×10 CM. FIELD; 85 CM. FOCAL-SKIN DISTANCE
Roentgens at point per 100 roentgens in air at position of axis of rotation

Points	Measured	1	2	3	4	5
		Isodose chart, 12 ADs	Isodose chart, Average AD	Central line, 12 ADs	Central line, Average AD	MIT
CENTRALIZED TUMOR						
A	39.6	41.0	41.0	41.0	41.0	40.5
B	41.0	42.9	43.4	45.8	45.8	44.4
C	40.0	40.5	40.5	43.4	43.4	43.4
D	42.0	43.4	43.9	46.3	46.3	44.9
E	40.5	40.5	40.5	43.4	43.4	42.9
Skin	30.9	28.0	28.9	25.6	26.5	26.0
ECCENTRIC TUMOR						
A	42.9	42.5	43.9	42.5	43.9	41.5
B	37.6	36.2	36.2	39.1	39.1	39.1
C	45.8	49.2	52.1	53.6	56.0	52.6
Skin	28.9	27.0	28.9	26.5	28.5	26.0

ogy plan. Of the four variants, it would be expected that the first should give the most accurate values, and the others successive degrees of approximation.

The results for the two cases are shown in Table IV. As expected, calculations on the basis of isodose contours and twelve average depths gave values in best agreement with measured ones. For all points in the centrally located tumor, the difference between calculated and measured values was less than 5 per cent; for the skin point, 10 per cent. For the eccentric tumor, the point (c) closest to the skin showed also a difference of 7 per cent. For the centrally located tumor, values calculated by all methods agreed within 12 per cent with the measured ones, and in most cases agreement was better. For the eccentrically located mass, values for a peripheral point showed more variation.

As a further check on the method here presented, for a number of actual cases, calculations were made by the four schemes outlined above, and compared with the values from the standard procedure in use at the Presbyterian Hospital, based on charts of the MIT type. These included three head cases, three in the thorax, and three in the abdomen. Each group included a central tumor, a moderately eccentric one, and a very eccentric one. In some cases rotation was complete, in others segmental scanning was used. In this latter group sometimes two segments were scanned, in other cases a fixed port on one side supplemented scanning on the other. In each case a single isodose chart was employed, based on the suitable average focal skin distance. In all instances (except for a few isolated skin points) doses calculated by the basic plan advanced in this paper (approximation four, number 1 in Table IV) agreed with the accepted values from the MIT type charts by better than 10 per cent, and the variations among results of all methods was only slightly greater than this. For central lesions it makes no difference whether an overall average depth is used, or twelve separate average values. With eccentric lesions in large parts of the body it appears preferable to use twelve separate depths and average the doses, rather than simply averaging depths. Values based on center

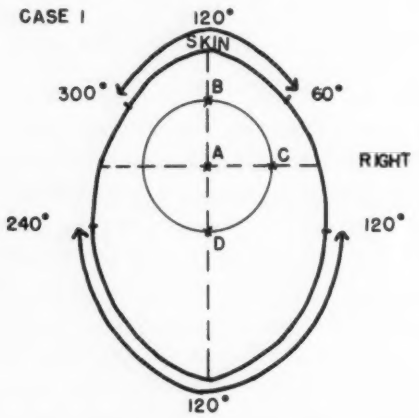
TABLE V—CASE 1

ECCENTRIC TUMOR (CARCINOMA OF PALATE), TREATED BY SCANNING ANTERIORLY OVER 120 DEGREES FROM 300° TO 60°, AND SCANNING POSTERIORLY TWICE AS LONG OVER 120° FROM 120° TO 240°: 250 KV. 1.5 MM. Cu HVL.; 5×5 CM. FIELD; 85 CM. FOCAL AXIS DISTANCE; 75 CM. AVERAGE FOCAL-SKIN DISTANCE

Roentgens at point per 100 roentgens in air at position of axis of rotation.

1	2	3	4	5	6
Points	MIT	Isodose chart, 10 ADs	Isodose chart, 2 average ADs (△)	Central line, 10 ADs	Central line, 2 average ADs (△)
A	47.8	49.2	49.7	48.7	48.3
B	54.5	51.6	51.6	54.1	54.5
C	51.6	49.2	49.7	54.1	53.1
D	46.8	45.4	45.4	47.8	47.3
Skin	19.8	19.8	19.3	21.2	20.7

(△) Two average air doses were taken corresponding to the anterior and posterior scanning.



line values rather than on isodose charts were somewhat higher, as would be expected. However, the difference between the two is only a few per cent except for points on the very periphery of the beam. While use of isodose charts is to be preferred, it appears that no serious errors will be introduced by using axial values if charts are not available. It is not practicable to give details of all these cases. Three which presented special problems are summarized in Table v.

All of the foregoing material has been based on the assumption of a fixed focal axis distance and the use of a number of isodose charts based on different average focal-skin distances. In practice the number of charts needed may be considerable because of various sizes and parts of the body. For a child's head (10 by 15 cm.) the average focal-skin distance would be 78.7 cm.; for the abdomen of a stout man (30 by 40 cm.) it would be 67.5 cm.; intermediate sizes would give intermediate values. Some selection must be made, with a certain degree of acceptable variation. If a focal axis distance of 85 cm. is employed, usually body contours can be handled satisfactorily with charts for 70 cm. distance and head contours with charts for

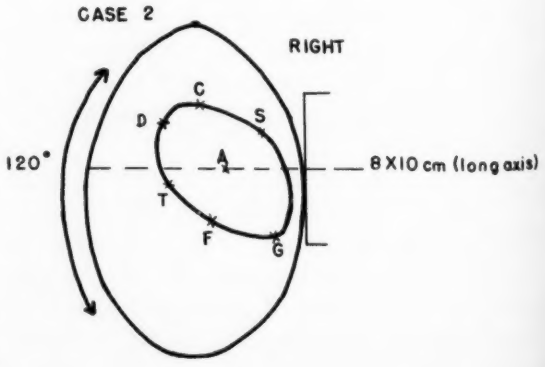
TABLE V—CASE 2

ECCENTRIC TUMOR (SQUAMOUS CARCINOMA OF THE NASOPHARYNX WITH EXTENSION INTO RIGHT EXTERNAL AUDITORY CANAL), TREATED BY SCANNING TO LEFT SIDE OVER 120° FROM 30° TO 150°, AND BY FIXED PORT TO THE RIGHT. SCANNING: 250 KV.; 1.5 MM. Cu HVL.; 8×8 CM. FIELD; 85 CM. AXIS FOCAL DISTANCE; 75 CM. AVERAGE FOCAL-SKIN DISTANCE. FIXED PORT: 200 KV.; 1.0 MM. Cu. HVL; 50 CM. FSD; 8×10 CM. FIELD

Roentgens at point per 100 roentgens in air at position of axis of rotation. Half of axis tumor dose delivered from each side.

1	2	3	4	5	6
Points	MIT	Isodose chart, 5 ADs	Isodose chart, average AD (△)	Central line, 5 ADs	Central line, average AD (△)
A	56.8	56.6	56.6	56.6	56.6
C	52.4	52.1	51.1	52.8	51.8
D	45.8	45.1	44.2	46.1	45.0
F	58.3	58.0	57.5	57.9	58.0
G	70.8	69.4	68.5	69.4	68.9
S	61.6	62.1	61.6	62.1	62.1
T	49.4	51.6	51.3	51.5	52.0
H (skin)	71.8	70.9	70.1	70.8	70.6

(△) An average air dose was used for columns 4 and 6; this average was taken from the five segments used for scanning.



80 cm. Possibly for the 70 cm. distance about 8 charts will be desirable, covering areas from 50 to 250 sq. cm., while for 80 cm. about 4 will be needed, for areas from 15 to 50 sq. cm. Any preferred focal-skin distance can be employed; for a distance different from 85 cm, the data here presented will have to be suitably modified.

If the rotation unit can be moved with respect to the roentgen tube, it is of course practicable to change the focal axis distance for patients of various sizes, so as to maintain a constant average focal-skin distance. This would eliminate minor errors, but would introduce another factor into the setting up of the patient. If the shift in distance between two patients' treatments were neglected, errors of much greater magnitude would be introduced than those involved in the use of slightly different distances.

If a constant focal-skin distance is to be maintained, the chart of Figure 5 would theoretically have to be modified, since K is 100 per cent of the axis dose *whatever the focal axis* distance. However, for the slight changes involved, no serious error will be introduced by using the chart as it stands. For example, if a shift to 78 cm. were made to treat a head case, the correct factor for 6 cm. depth would be 1.17, while that from the chart is 1.16. While the method of a fixed average focal-skin distance has a certain appeal, it is probably less desirable from a practical point of view. The possibility is worth mentioning, but the procedure is not in general advised.

ABSTRACT OF PROCEDURE FOR BEST APPROXIMATION

1. Make a contour of the region to be treated, on translucent paper or vellum.
2. On this contour, mark the region of the tumor. Localization films are usually essential for this.
3. Place this contour over a celluloid base marked off in polar coordinate form.
4. On a suitable tabular form (see Table III) list the 12 values of T, the distance from the skin to the center of rotation, one for each 30 degree segment.

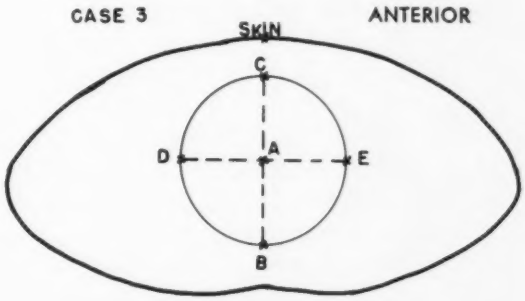
TABLE V—CASE 3

CENTRALIZED TUMOR (CARCINOMA OF LUNG). PATIENT TREATED BY COMPLETE ROTATION WITH THE ARMS DOWN: 250 KV.; 1.5 MM. CU. HVL; 10×10 CM. FIELD; 85 CM. FOCAL AXIS DISTANCE; 72.5 CM. AVERAGE FOCAL-SKIN DISTANCE

Roentgens at point per 100 roentgens in air at position of axis of rotation.

1	2	3	4	5	6
Points	MIT	Isodose chart, 12 ADs	Isodose chart, average AD (△)	Central line, 12 ADs	Central line, average AD (△)
A	52.6	52.1	54.1	52.1	54.1
B	51.2	59.4	60.8	53.6	55.5
C	62.3	58.4	61.3	61.8	64.7
D	54.1	47.8	58.4	53.1	54.5
E	55.5	48.3	58.9	55.5	57.0
Skin	36.2	40.0	43.4	38.6	42.0

(△) The average air dose taken for columns 4 and 6 corresponds to 12 segments because of complete rotation.



5. Using these twelve distances and the inverse square chart (Fig. 5) obtain and record the twelve 100 per cent air doses.
6. Using the appropriate isodose chart, correctly centered over the axis of each segment, record the instantaneous percentage depth doses for each point under consideration.
7. Multiply each percentage depth dose by its corresponding 100 per cent air dose, to obtain the instantaneous tissue dose.
8. Take the average of all these partial tissue doses; this is the dose delivered to the point per 100 roentgens in air at the distance of the axis of rotation.

DISCUSSION

At this point mention should be made of a factor which appears to have been neglected in previous considerations, although actually this has not introduced appreciable

errors. Published depth dose tables and isodose charts have been developed from careful measurements in unit density phantoms with flat surfaces. For strict accuracy in dosage calculations the patient should also present a flat surface to the beam. This is rarely the case. For treatment with stationary ports, bolus material is used to pad out irregular surfaces, thus justifying the use of standard isodose charts. In rotation, flat surfaces are unobtainable, because of the very nature of the physical motions and contours involved. As a consequence, the instantaneous representation of the isodose distribution in space would be asymmetrical with respect to the central ray.

It has been shown[2] that the dose along the central axis, for a field striking a surface obliquely, is the same as for a field striking a surface perpendicularly. It is further shown[3] that the isodose curves near the center of the field are inclined at an angle approximately half way between the perdicular to the axis and a line parallel to the skin. Thus for the instantaneous tilted position, standard dosage charts are not strictly applicable. However, since the human body is relatively symmetrical, and the actual tilts are not very great, a particular tilt, at one instant, with its resultant isodose distortion, is compensated for at another instant by an opposing type of distortion.

SUMMARY

Methods are presented for calculating tissue doses in rotation therapy, based on standard isodose charts available in any radiotherapy department. Calculations are simpler and more expeditious than for methods previously published.

In certain cases, calculated doses have been checked by measurements in phantoms shaped to represent the appropriate part of the body; the agreement is excellent.

The authors wish to express their thanks to Miss Beverly Singer and Mrs. Lia Merenfeld for assistance in making some of the calculations. The work was made possible by a grant from the American Cancer Society, to whom grateful acknowledgment is made.

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THE EFFECTS OF GAMMA AND ROENTGEN RADIATION ON THE INTACT SPINAL CORD OF THE MONKEY

AN EXPERIMENTAL STUDY*†

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INTENSIVE irradiation provides at the present time the most favorable means of treatment for certain neoplasms of the central nervous system. It seems essential, therefore, that the tolerance of normal neural tissue to this type of therapy be established as accurately as possible. The availability of artificially radioactive materials has made possible experimental studies directed toward this end.

There were three principal objectives in this work. The first of these was to reassess the clinical and histological effect of radiation on nervous tissue in terms of present day concepts of dosimetry. The second purpose was to attempt a qualitative and quantitative comparison between gamma and roentgen radiation as regards dosimetry, tolerance and histological response. The third objective was to establish the tolerance of normal neural tissue to rapid intensive irradiation as a basis for the possible use of artificial radioactivity in the treatment of tumors.

The spinal cord was chosen as a favorable part of the nervous system for this study for two reasons: (1) the relatively small size of the cord permits more accurate measurement of the radiation delivered and greater uniformity of the dose; (2) damage to the spinal cord can be more accurately appraised clinically because of the concentration of functional components in a small area as compared with more diffuse cerebral representation.

Few previous observations have been made on the reaction of the spinal cord to radiation. These have been scattered over many years and have included experiences with different sources and types of radiation. (1) Pendergrass, Hayman, Houser and Rambo[7] (1922) applied radium to the spinal cord of 4 dogs and gave results in terms of milligram hours' exposure; 600 mg. hr. was found to produce weakness progressing to total paralysis within six weeks; (2) Cairns and Fulton[1] (1930) placed radon seeds dorsal to cords of cats and monkeys. Results were interpreted in terms of millicuries and certain dosages were found which produced complete, incomplete or no paralysis. Monkeys were found to be more resistant to radiation, only slight weakness being produced by 12 millicures. (3) Peyton[8] (1934) placed gold radon seeds around the periphery of the spinal cord in dogs and noted that the latent period between implantation and onset of paralysis decreased with increasing dosage. Different quantities of radon were placed in the animals, however, so that there was no uniformity of rate of delivery of radiation. (4) Davidoff, Dyke, Elsberg and Tarlov[3] (1938) exposed the cords of 3 monkeys to roentgen radiation and found that a single dose of 5,000 roentgens produced immediate paralysis and death. This, as will be noted later, is in contrast to a somewhat greater tolerance found in the present study.

Not only have different sources and types of radiation been used but the results have been expressed in various units of measurement. Because of the lack of certain data from these earlier studies it is impossible to make an accurate compari-

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TABLE I

PROPERTIES OF TANTALUM 182

Beta radiation
Energy 0.53 mev.
Range (unshielded) 2 mm. in soft tissue, maximum

Gamma radiation

Mev.	r/mc. hr. at 1 cm. in air	Relative Intensity	Contribution (r)
1.22	6.6	0.57	3.762
1.13	6.22	0.37	2.301
0.22	1.2	0.04	0.048
0.15	0.67	0.02	0.013
Total gamma dose (r/mc. hr. at 1 cm. in air)			6.124

Half-life 117 days

son of results. With increased understanding of the nature of radium emanation it has become possible to employ a unit (the roentgen) which is essentially interchangeable between gamma and roentgen radiation. The emphasis in previous investigations has been on the total dose administered rather than the rate of delivery. As will be stressed in this report, the early effect of irradiation is primarily related to rate of administration.

METHODS

In this study a total of 35 *Macacus rhesus* monkeys has been used. Eighteen of these have received gamma radiation and the remaining 17 received roentgen radiation to the spinal cord in the lower dorsal region.

Tantalum wires, each 1 centimeter long, irradiated in the atomic pile at Oak Ridge and encased in polyethylene, were used as the source of gamma radiation. The nonreactivity of both tantalum and polyethylene with normal nervous tissue has been previously established.[2,4,5,9,10] The characteristics of radioactive tantalum (Ta^{182}) are shown in Table I. The beta particles are of such energy (0.53 million electron volts) that they can be easily shielded by sealing the tantalum in a polyethylene tube, or, if not shielded, the beta radiation is completely absorbed at a distance of 2.0 mm. from the source. The half-life is 117 days, indicating that during the time of exposure of most of our animals there was minimal change in the intensity and rate of irradiation. The tantalum wires were placed extradurally on the dorsal surface of the cord in most animals, but in a few they were placed beneath the skin in the posterior midline fixed to the paravertebral fascia. This latter placement removed the source from the cord, thereby creating more uniform irradiation of the cord, but had the disadvantage of delivering a tremendously large dose to the immediately overlying skin and producing subsequent necrosis. The dosage calculations have been made relative to the center of the cord and were based on the position of the tantalum, as demonstrated on roentgenogram, and on the actual thickness of the cord measured at autopsy.

The 17 animals that received roentgen radiation were also treated in the lower dorsal region. The exact level of treatment was determined by a roentgenogram in each case. Roentgen radiation was delivered through a 2 by 2.5 cm. port at 125 kv., 5 ma., tube-skin distance 15 cm., filtered through 1 mm. aluminum. The rate of delivery of the roentgen radiation to the center of the spinal cord was 138 r per minute. The radiation was given while the animals were under pentothal or nembutal anesthesia.

RESULTS

Clinical Observations. With respect to both gamma and roentgen radiation it was apparent that the occurrence and severity of early paralysis was a function primarily of the rate at which radiation was delivered, the total dose being of secondary importance.

The 18 animals which received gamma radiation are summarized in Table II and are listed in order of increasing rate of administration. In all animals which received radiation more rapidly than 135 r per hour some degree of paraplegia developed. Two animals which received radiation at a rate less than 135 r/hour exhibited paralysis subsequent to extensive ulceration and infection of the soft tissues of the back. It cannnot be assumed, therefore, that this deficit was the result of irradiation alone. The appearance of disability occurred late in these animals and, as will be noted later, did not appear at the time

TABLE II

TANTALUM IRRADIATED ANIMALS

Animal	r/hr.	Total r	Result (paralysis)	Animal	r/hr.	Total r	Result (paralysis)
M-15	1.1	213	o	M-9	129	3,100	o
M-17	1.9	6,026	o	M-21	131	9,460	o
M-18	3.9	5,606	*	M-8	132	6,250	o
M-22	10.5	10,000	*	M-6	135	3,100	++
M-44	55	38,088	o	M-4	140	3,220	+++
M-30	65	18,016	++	M-3	143	6,220	+
M-46	119	37,838	++++	M-2	147	4,420	+
M-11	125	3,120	o	M-71	172	8,215	++
M-10	126	3,080	o	M-70	185	12,048	++++

* Developed extensive soft tissue ulceration.

when an acute radiation effect would be expected. Two other animals (M-30 and M-46) showed evidence of spinal cord damage only after relatively large total doses. It should be pointed out that in M-30 a transient mild paraplegia occurred which cleared during the subsequent three months and has not recurred up to the present time, one year later. The remaining animals showed no clinical effect of the irradiation.

The importance of the rate of administration of gamma radiation is illustrated by the group of animals consisting of M-11, M-10, M-9, M-6 and M-4. Each of these received approximately 3,100 r as a total dose. The rate varied from 125 r/hour to 135 r/hour. The three animals irradiated at a rate less than 135 r/hour showed no effect while the remaining 2 animals developed early clinical paralysis. Consideration of these 5 animals indicates that a critical rate of delivery exists relative to the tolerance of the spinal cord.

In the animals treated by roentgen radiation it was also observed that early neurological damage was a function primarily of the dosage delivered per day. The 17 animals treated in this manner are listed in Table III in order of increasing rate of administration. It is apparent that although quite large total doses could be administered there was no paralysis if the dosage rate was 3,000 r/day or less. Thus, as much as 15,000 or 22,500 r could be given without ill effect. On the other hand, 5,000 r was the maximum single dose which could be tolerated by most animals. If this was repeated on the following day clinical loss of

TABLE III

ROENTGEN IRRADIATED ANIMALS

Animal	r/day	Total r	Result (paralysis)	Animal	r/day	Total r	Result (paralysis)
M-24	1,330	4,000	o	M-37	5,000	15,000	+++
M-25	1,330	4,000	o	M-43	7,500	7,500	++++
M-28	1,500	22,500	o	M-45	7,500	7,500	o
M-41	3,000	15,000	o	M-47	7,500	7,500	++++
M-19	4,000	4,000	o	M-48	7,500	7,500	o*
M-42	5,000	5,000	o	M-49	8,500	8,500	++++
M-26	5,000	5,000	o	M-50	8,500	8,500	o*
M-38	5,000	10,000	++	M-51	8,500	8,500	o*
M-40	5,000	10,000	+++				

* Sacrificed before paralysis could occur.

function occurred. A single dose of 7,500 r or more was found to produce paraplegia consistently. Only 1 animal out of 7 treated with this tremendous single dose remained unparalyzed.

The paralysis usually made its appearance with four days. The only animals developing paraplegia more than ten days after the beginning of either gamma or roentgen irradiation were the two monkeys whose paraplegia occurred subsequent to extensive skin ulceration. Indeed, only 1 animal showed a progression of the severity of paralysis after the first two weeks. In this animal paralysis increased in severity up to about four months, at which time there was an estimated 75 per cent loss of function, followed by slow but steady improvement.

The variation in time of onset of paralysis during the first week was related to the rate of administration, paralysis occurring sooner in those animals given the most rapid irradiation. The deficit occurred with amazing rapidity, usually over a period of one to three hours. If the paralysis was not complete during these first few days it was usually of a spastic type with adduction and extension of the legs. If, however, the paralysis was complete, as happened after a large single dose of roentgen radiation, it was flaccid. The flaccidity persisted for at least nine days, which was the longest time a totally paraplegic animal was allowed to survive. In most instances they were sacrificed within a week for purposes of histological study or at the time of electrical studies of the cord. It is interesting to speculate whether the persistence of flaccidity following complete transection of the cord by irradiation indicates continuance of a state of spinal shock which should subside in monkeys in several hours or at most in a few days. Although histological changes were seen caudad to the segment of spinal cord exposed to the most intensive irradiation, the relatively normal electrical activity below the site of irradiation suggests that the persistent flaccidity was not due to spread of the radiation effect to this region. Following the initial appearance of paralysis, the deficit increased in severity during the next week. After this time gradual improvement occurred up to the time of spontaneous death or sacrifice.

Relatively few animals survived for long periods. Many of them were sacrificed soon after irradiation to study the early histological effects. The animals which became totally paraplegic succumbed within seven to ten days, probably from overwhelming sepsis resulting from either urinary tract infection or decubiti. A third group of 5 animals died within two to four months, apparently from the effects of irradiation on the abdominal viscera. These animals had all been given roentgen radiation varying from 4,000 to 10,000 r. At necropsy they usually showed some abdominal distention, apparent atony of the colon, peritoneal effusion in 3 instances, hyperemia of the bowel wall, and in 1 case bleeding into the lumen of the gastrointestinal tract. At present 4 animals of the tantalum irradiated group are living, including 1 which had received 18,000 r to the center of the spinal cord thirteen months ago. Another animal received 8,200 r eighteen months ago (the longest survival to date) and recovered from an early neurological loss with no apparent residual deficit at the present time. Each of the 4 animals has received over 6,000 r to the cord and it seems possible that late progressive vascular changes with resultant cord damage may be anticipated.

Neurophysiological Observations. Three methods of electrical testing have been used in selected animals:

(1) Cord-to-cord recordings of conducted impulses have been obtained by implanting electrodes several millimeters into the dorsal cord under nembutal anesthesia. The stimulating and recording sets of electrodes were then moved up or down the cord maintaining the same distance between them. The cephalad electrodes were stimulated by a square wave current of 0.2 milliseconds' duration and 0.8 volts. The recording electrodes were led through an amplifier to an oscilloscope. Stimuli were applied at one second intervals.

Normal impulses were recorded above the irradiated area. In those animals rendered paraplegic by a massive dose of radiation, no impulses were obtained within the irradiated zone which extended approximately 4 cm. in length, *i.e.*, somewhat more extensive than the longitudinal dimension of the portal employed. Furthermore axon potentials were obtained below the irradiated area, indicating that under these rather artificial conditions conduction below the area was intact. The tests were performed one week after irradiation and four days after onset of paraplegia at which time the animal still showed a flaccid paralysis.

Another animal which had received 7,500 r of roentgen radiation but which, apparently as a result of individual variation in susceptibility to radiation, had not become paralyzed was tested in a similar manner. This animal showed normal cord-to-cord conduction potentials above, below and within the irradiated segment (Fig. 1).

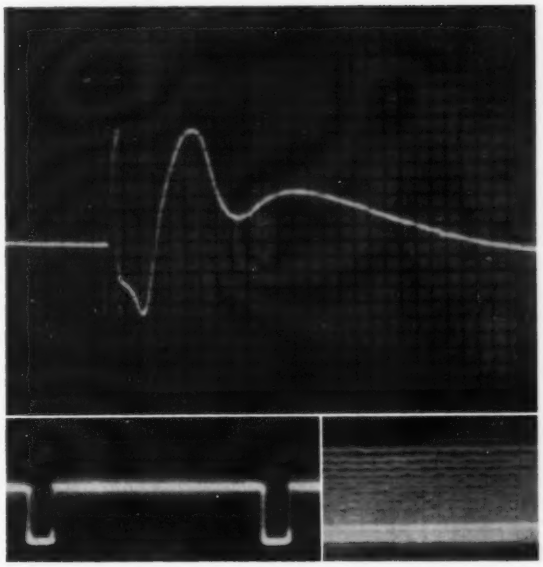

Fig. 1. Oscilloscopic recording of impulse transmitted across irradiated segment of spinal cord of animal which had received 7,500 r roentgen radiation. This configuration was repeated within the nonirradiated cord above and below the irradiated area. Calibration signals: Time, 500/second; amplitude, 0.2 millivolt.

(2) Spinal electrograms were made, using steel needle electrodes and recording on a Grass electroencephalograph, to study the relative susceptibility of the nerve cell bodies and the axons.

In the normal monkey, the greatest amplitude of activity occurred at about the level of L1–2 vertebrae (Fig. 2*A*). The amplitude gradually diminished cephalad to the lumbar enlargement and the artefact produced by cardiac activity increased. There were, however, still recognizable spinal cord potentials in the lower thoracic levels, the region in which irradiation was carried out.

In an animal made paraplegic by roentgen irradiation there was complete absence of activity in the involved segment of spinal cord in contrast to normal activity above and below the irradiated region (Fig. 2*B*). In this animal the test was carried out nine days after irradiation and seven days following onset of total paraplegia. At the time of testing, the area visibly affected by the irradiation was 3.5 cm. long. Spinal cord potentials, however, were absent in a segment approximately 4.5–6 cm. in length. As the electrodes were gradually moved out of this region the normal spinal cord activity returned. This suggested that paraplegic doses of radiation not only block the long conduction systems but depress the activity of the cell bodies simultaneously.

The possibility of increased susceptibility of the cell bodies to irradiation was investigated in two animals. One of these was an animal treated with 7,500 r roentgen radiation (the only animal to receive this dose without subsequent paraplegia) and the second had a transient paraplegia. The former was tested at nine days and the latter four months after irradiation. In both instances essentially normal activity within the irradiated region was present (Fig. 2*C*).

(3) As further test of the susceptibility of cell bodies, the posterior to anterior root reflex arc was studied oscillographically in an animal which had received 5,000 r roentgen radiation to the lower spinal cord, an amount just below the paralyzing dose. There was no evidence of weakness or sensory loss in the lower extremities. The

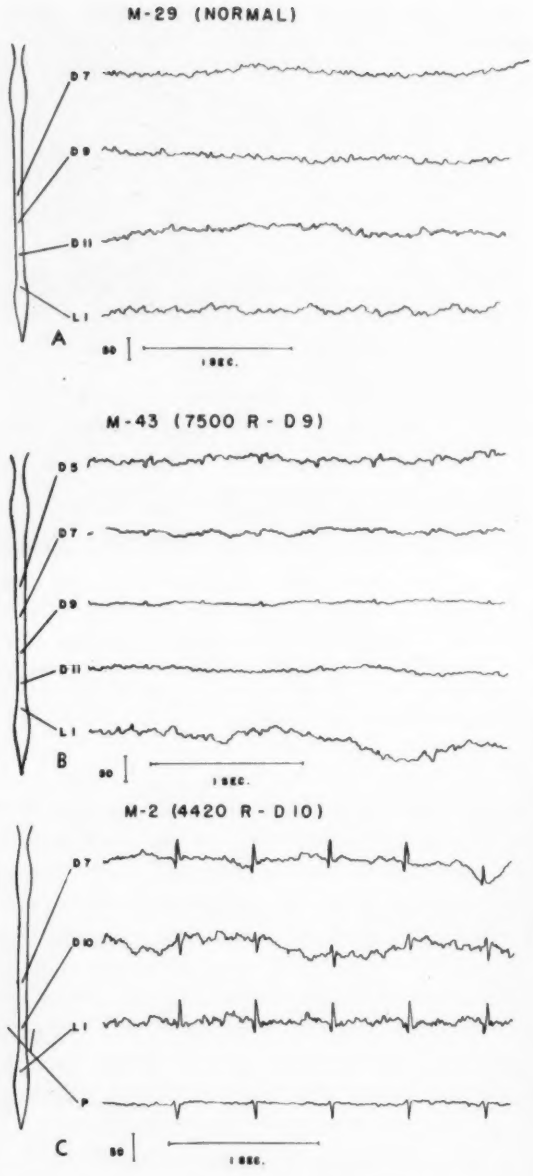

FIG. 2. Spinal electrogram. (*A*) Normal monkey. Note decreasing amplitude of potentials as the electrodes were removed from the lumbar enlargement. (*B*) M-43, rendered paraplegic by 7,500 r roentgen radiation. Note almost total absence of cord activity at level of irradiation and progressive return of activity as the nonirradiated cord was approached. (*C*) M-2, rendered partially paralyzed by 4,420 r gamma radiation followed by complete recovery. Note presence of normal activity and superimposed electrocardiogram within irradiated segment. The contribution of paravertebral leads is also shown.

reflex arc was tested using a 1.3 volt 1.0 millisecond stimulus to the posterior root. A normal monosynaptic response was obtained, indicating functional competence of the primary reflex arc (Fig. 3). The polysynaptic response was not clearly recorded but on the basis of one experiment no valid conclusions can be drawn about the effect of radiation on the internuncial pool.

PATHOLOGIC STUDIES

Methods. The brain and spinal cord of all animals were immediately removed at the time of spontaneous death or sacrifice and fixed in 10 per cent formalin, the dural coverings being kept intact. After fixation the dura was removed and the cerebrospinal axis of each specimen inspected.

Histopathological studies were carried out at multiple levels of the spinal cords, and in selected areas of the brains. A preliminary survey was made by the use of sections from paraffin-embedded material stained with hematoxylin and eosin, Mallory's phosphotungstic acid-hematoxylin,

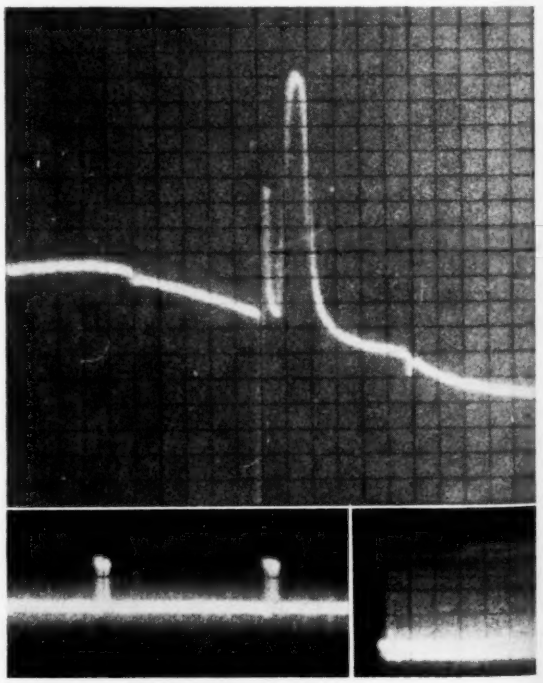

FIG. 3. Oscilloscopic recording of posteroanterior root reflex arc within irradiated segment of animal which received 500 r roentgen radiation. The characteristic monosynaptic response is shown without a well defined polysynaptic response. Calibration signals: Time, 500/second; amplitude, 0.5 millivolt.

and Sudan black for myelin. On the basis of this survey other selected methods were used as required. Since the present report is devoted chiefly to clinical and neurophysiological aspects of irradiation only a brief summary of the pathological changes is included. A full report will be published elsewhere.

Gross. Softening and diminished vacularity of the cord were the only gross changes identified. These changes were more prominent in the animals which had become paraplegic and which had survived for considerable intervals after irradiation. They were limited to two or three segments of the spinal cord.

Histopathology. The histopathologically identifiable damage clearly depended on two factors: the length of survival after irradiation and the total amount of radiation received. The former was the more important of the two, indicating the progressive nature of the reaction.

In the spinal cords of monkeys receiving the largest doses of radiation and allowed to survive for several months, total necrosis and disruption of both white and gray matter were found. The spinal arteries in the fibrosed and hyalinized meninges presented extensive intimal proliferation which in some instances progressed to complete occlusion. The intramedullary lesions could thus be regarded as a transvere infarction at the level of irradiation.

The pathogenesis of the arterial change was followed by comparing the findings in several monkeys of the series. At the earliest stages after irradiation the arteries appeared essentially normal. Later there were necrosis of the vessel walls and inflammatory cellular infiltration. This state was followed by healing and development of occlusive endothelial proliferation. At successive levels cephalad and caudad to the region of transverse infarction, the vascular changes became progressively less pronounced. The tissues of the spinal cord showed greater injury to the white matter than the gray. There was a marked glial proliferation in the areas of damage to the white matter. Below the area of maximum injury some of the changes were undoubtedly due to retrograde degeneration but the similarity of many of them to changes above the site of irradiation suggested that a direct radiation effect was also present.

In contrast with the picture described above, the monkeys receiving equivalent dosages of radiation and sacrificed a few days later presented a relatively normal appearance. In the white matter a few myelin sheaths were swollen and partly degenerated; no morphological change was recognized in the gray matter.

From the material it appeared that the lesions resulting in paraplegia were primarily vascular in origin but that injury to neurones extended for considerable distances beyond the area of maximum irradiation. The white matter was more affected than the gray. The extent and distribution of the lesions were considered an indication that gamma and roentgen radiation can injure the nerve fibers directly without mediation of vascular lesions.

Since the histopathological changes were greatly increased in severity with time, the injury was a continuing phenomenon, or at least one which was progressively more unmasked histologically with time.

In comparing the effects of gamma radiation with roentgen radiation it appeared that the two agents produced essentially the same types of reaction but that those due to gamma radiation were somewhat more severe.

DISCUSSION

The greater resistance of nerve tissue to irradiation relative to other tissues of the body has long been appreciated. The present findings are in agreement with this with respect to both gamma and roentgen radiation. They demonstrate, however, the importance of the rate of administration when one is dealing with an intensive source of artificial radioactivity. They also indicate the specific rate at which the gamma radiation from tantalum is tolerated by the nervous tissue. Furthermore, this work reveals that extremely large

single doses of roentgen radiation may be tolerated for at least several months. Even larger total doses given by the fractionated method may be tolerated.

On the basis of the available data from the animals treated with roentgen radiation, it is not possible to construct a complete curve for the dose-time relationship as has been done by previous workers for skin tolerance.[6] A few points on the curve, however, may be obtained. A single dose of 7,500 r results in paraplegia while two doses of 5,000 r each are required. If 3000 r is administered per day no effect occurs up to a total of 15,000 r. If, then, 3,000 r is considered a tolerable daily dose from which the nervous tissue can recover sufficiently in twenty-four hours to prevent irreparable damage, a rough relationship can be established between this and the tolerance of gamma radiation. It was pointed out that 135 r/hour was the maximum rate at which gamma radiation could be administered without the appearance of early damage. If this is calculated for a twenty-four hour period the tolerance would be approximately 3,250 r/day, or slightly greater than the tolerance to 125 kv. roentgen radiation. This is consistent with the work of other investigators who found that to produce skin erythema a greater amount of high voltage roentgen radiation was required than low voltage radiation. In the present studies the radiation from activated tantalum has a much higher energy than the roentgen radiation employed.

It is beyond the scope of this work to examine the theoretical aspects of the effects of ionizing radiation on normal nervous tissue. It is probable, of course, that the methods of action of gamma and roentgen radiation on living cells are identical. As pointed out previously the histological damage is qualitatively similar in the two groups of animals.

The objective of these studies has been to establish a few facts regarding the reaction of normal nervous tissue as a basis for possible use of artificial radioactivity in the treatment of tumors of the nervous system. To this end similar experiments are being carried out on normal cerebral tissue. It is hoped that a satisfactory method may be developed to determine the optimum rate of irradiation to produce the most profound effect on neoplastic tissue of nervous origin.

The results of our work are at some variance with those of Davidoff *et al.*,[3] who found that in the monkey 5,000 r produced immediate paraplegia and death in three days. In the present study 5,000 r was consistently ineffective as a single dose. It is difficult to reconcile these two sets of observations, for it would be expected that the greater kilovoltage used by Davidoff's group would result in an even higher tolerance than that obtained in this work. It is significant, however, that only one animal was given that amount of radiation by those observers. Differences in biological response have been found several times in the present series.

Peyton's data obtained from placing gold radon seeds around the periphery of the spinal cord again shows the close relationship between the severity of injury and the rate of administration. The dogs under observation became paralyzed much more rapidly by 5 mc. of radon than by 2.8 cm. even though the total dose was greater in the latter instance.[8]

The end point of our studies on tolerance of the spinal cord has been paralysis occuring during the first few days after treatment. To determine what factors were responsible for this early damage animals were sacrificed twelve, twenty-four and forty-eight hours after a paralyzing dose of roentgen radiation. Those sacrificed at twelve and twenty-four hours were in the pre-paralytic stage while the one at forty-eight hours was totally paraplegic at the time of death. Histologically it was not possible to determine any severe structural changes in these animals. It must be concluded, then, that either there is a purely functional alteration of the nerve cells without visible evidence of injury or the

disruption of cord function results from massive vasospasm which cannot be detected in the postmortem specimens. Some support for the latter theory is derived from the sudden onset of the paralysis and from the lack of evidence of differential susceptibility between the cell bodies and the conduction pathways in the electrical studies described.

The late appearance of radiation effects has been known for years, and several reports have described instances of late paraplegia following roentgen therapy to tumors of the neck or paraspinal region. These late effects have usually appeared twelve to eighteen months after irradiation. It is interesting that of the 4 animals in this study which are surviving at present no late effects have been noted, although 2 of these received 18,000 r and 8,000 r and have lived thirteen and eighteen months respectively.

SUMMARY

Thirty-five *Macacus rhesus* monkeys have been subjected to gamma radiation from radioactive tantalum or roentgen radiation of the spinal cord. The effects of these two agents were compared qualitatively and quantitatively in normal nervous tissue. The study was also intended to provide a basis for further study of intensive irradiation in the therapy of nervous system tumors.

The early effect of radiation is a function primarily of the rate of administration and secondarily of the total dose. The tolerance of the spinal cord to gamma radiation of the energy used in these experiments is approximately 135 roentgens per hour. The tolerance of 125 kv. roentgen radiation is less well defined but is probably somewhat lower than that found for gamma radiation.

Electrical observations on the irradiated spinal cords indicate simultaneous suppression of function of nerve cell bodies and axons during the early radiation reaction. This suggests that a vascular mechanism is responsible for the early damage.

Histological changes are either minimal or absent during the early reaction to radiation. Later studies show progressive vascular damage as well as changes of the gray and white matter attributed to a direct radiation effect. The histological effects of gamma radiation are qualitatively similar to those resulting from roentgen radiation but are somewhat more severe.

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BIOLOGICAL MODIFICATION OF EFFECTS OF ROENTGEN RAYS*

II. HIGH TEMPERATURE AND RELATED FACTORS

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THE utmost advances in radiation technology cannot overcome the deficiencies of biological selectivity which now rank radiotherapy below surgery for most major neoplasms. Biological reactivity dominated the preceding study of tumor ligations.[1] Wood[2] stated: "The morphological changes which accompany the destruction of tumor cells by x-rays or gamma rays have been shown by myself and others not to be characteristic of these radiations but an effect common with other physical agents, such as heat and cold, on the cell." The writer's previous investigations of thermal influences,[1h,j,n] including reduced temperature,[1m] are here continued with respect to elevated temperature.

With 250 kv. apparatus, the physical constants and general methods have been the same as in the preceding observations.[1m] Space limitations have compelled omission of experimental details in the form of either descriptions or tables. The procedures are so simple that the results can be adequately conveyed in brief summaries.

A. EFFECTS OF GENERAL AND LOCAL IRRADIATION OF NORMAL RATS

1. Single Treatments

Local tolerances conformed to the previous reports:[1d,m] for tails, approximately 3,000 r for erythema, and increase of damage with dosage up to mummification and self-amputation with 3,500–4,000 r; for legs, slight vesication and temporary epilation with 3,500–4,000 r and gangrene with about 6,000 r. With 4,000–4,500 r, ulceration extending from the sensitive foot may cause loss of the leg; but if the foot is shielded such doses are tolerated with only permanent epilation and some muscle wasting and joint changes.

The results of whole body irradiation differed slightly from those previously described, in that rats at normal temperature were killed not only by 1,250 r but occasionally by lower doses down to 850 r, the cachectic decline then lasting two or three weeks. Variability may have been accounted for by different strains of rats or the use of a different machine delivering the same calculated dosage.

Comment. The existing literature on roentgen-ray damage has not sufficiently noticed certain details. (a) Systemic: Latency is brief. The quick death from overwhelming dosage is familiar. With more moderate doses, the rats act well for twenty-four to forty-eight hours; then failing appetite and cachectic decline continue for a number of days or weeks, until death or recovery, though anatomic changes may be slight. There is thus a similarity to radiation sickness in man. (b) Local: Latency is long. A leg or tail remains apparently normal for two weeks, even after a radiation dose sufficient to destroy it. Then redness, vesication and other inflammatory changes begin and reach a maximum within the next two weeks, the final result being loss by deep ulceration or mummification, or healing lasting several weeks or months, followed by permanent epilation and fibrosis in severe cases. General physiological processes being more rapid in the rat, it is questionable whether the true erythema consists in the slight early capillary alterations which some writers have described,[3]

* The costs of this investigation were paid by Messrs. Harry and Moe Rediker of New York. Thanks are due to Dr. Milton Friedman for granting facilities, and to Dr. Frank K. Safford for invaluable aid throughout the entire work.

and whether the grossly visible "erythema" corresponds to the degenerative stage in man. These time differences between whole body (or visceral) and peripheral tissue irradiation will be found to exhibit some interest in connection with tumors.

II. Fractionated Treatments

The experiments of Henshaw and others previously cited were designed to determine safe tolerance limits for workers with radiation, or for other experimental purposes. There seems to be a total lack of observations on tissue tolerance of rats for radiation in such dosage and timing as might be used for tumor treatment by fractionation. The following notes are based on gross changes without microscopic checks.

Extremities. Totals up to 6,000 r, in doses of 1,000 r distributed through six months, failed to alter rats' legs noticeably. The same was true of 3,600 r given to tails in 600 r doses.

More complicated conditions were created when border line doses of 3,000 or 4,000 r were followed by smaller doses, usually 1,000 r, at various intervals, or vice versa. For example, a rat received 3,000 r on a hind leg, was allowed six weeks for recovery, then received six doses of 1,000 r distributed through six months to make a total of 9,000 r, with the result of only partial epilation of a fully functional leg. A considerable series established the conclusion that effects are not governed solely by the total amount of dosage, but are greatly modified by: (a) the size and timing of individual doses, the larger doses requiring longer times for recovery: (b) persisting lesions from an earlier dose, which sensitize very powerfully; (c) the reduced tissue resistance which accompanies malnutrition.

Pelvic Organs. Single irradiations of 3,000 r, or three doses of 1,000 r two or three weeks apart, caused moderate gross atrophy of rat testes, not checked by microscopic or fertility tests. Similar treatments to the pelvis of females were rather surprisingly ineffective, and one rat which received 3,000 r on May 4 was found pregnant in July and reared 8 healthy young. But the delicate skin of the posterior abdomen or scrotum shows beginning erythema and vesication with 2,000–2,500 r.

Whole Body Irradiations. The summation of effects of rapidly repeated doses is familiar, but a peculiar sensitization over longer periods has not been described heretofore. For example, an irradiation of 1,000 r may cause slight and transitory weight loss. But death results from the same dose six or eight weeks later, or from a third dose of 500 r after a similar interval, though the rat then has full weight and liveliness and no anemia.

Liver and Intestine. The well known resistance of the liver to radiation was illustrated by the absence of gross changes after as much as five doses of 500 r in three weeks, death occurring from pneumonia presumably from spread of the radiation. Similar dosage to the abdomen with shielding of liver and spleen caused no loss of weight or liveliness and no gross intestinal lesions. These results correspond to the general high resistance of rat tissues and indicate that hepatic or intestinal damage is not the cause of the anorexia, cachexia and death following whole body irradiation.

B. Roentgen Treatments of Rat Sarcoma

These experiments employed the Crocker sarcoma No. 39, which, according to my previous observations, reacts to various treatments in practically the same way as other common transplantable sarcomas or carcinomas of the rat. They are radioresistant in the sense that recession, though sometimes very extensive, is regularly followed by recurrence. Therefore the strict criterion of cure was the permanent survival of a tumor-free animal. Three special points in the methods may be noticed. (a) The tumors were implanted in legs or tails, which are more convenient for localized radiation than the customary

location along the side of the body. (b) Mature tumors have been used, namely leg tumors more than two weeks old having diameters of 2 to 4 cm., and tail tumors four to six weeks old. Necrosis of such tumors carries danger of loss of the part or death from systemic intoxication. This danger has not been much reduced by extruding the necrotic center or trimming superficial portions preparatory to treatment. But cures are more significant than in the case of a young graft struggling for a blood supply especially amid loose areolar tissue of the axilla. (c) With Sugiura's skillful management, axillary sarcomas in mice have been killed by as little as 1,500 r in vivo but require nearly twice this dose (about 2,800 r) in vitro. Against specific systemic influences on cells, the most probable explanation is the vulnerability of the mouse tumor stroma and capillaries. Also, contrary to Wood's unsupported assumption that anything that can cure the mouse sarcoma 180 will also cure human cancer, this sarcoma has been cured even by starch injections[5] and has been sensitized to radiation by mere injection of water.[6] Rat tumors have no such misleading vulnerability, and have a resistance to all therapy equalling or exceeding that of human tumors. Therefore cures, though few, are significant in that they have always been reproducible clinically,[1c,k] while the many false hopes aroused by mouse experiments should go far to discredit that animal as an object of therapeutic research.

Excluding numerous accidental deaths, the results in 73 rat sarcomas were as follows.

I. Single Irradiations of Rat Sarcoma

One dose of 6,000 r destroys a rat's leg. Absence of sarcoma from the large ulcer is meaningless, as part of an indiscriminate tissue necrosis. Doses of 4,000 to 5,000 r, which can be tolerated by the normal leg if the foot is shielded, destroy a tumor-bearing leg because ulceration extending from the tumor destroys blood vessels and bone; but the huge ulcer at the hip still contains sarcoma. With somewhat smaller tumors and radiation of 3,500–4,500 r there may be extensive tumor recession and distinct lengthening of the animal's life, but never cure. Dosage below 3,000 or 2,000 r has little effect on leg tumors. In the tail, where the normal tolerance limit is lower, doses of 2,000 to 3,000 r may cause separation at the tumor site, leaving sarcoma in the stump.

The most striking phenomenon in these occurrences has remained unnoticed in the literature; namely, the immediate action on the tumor contrasting with the latent period for normal peripheral tissues. Recession or ulceration of the tumor becomes evident within twenty-four or forty-eight hours and continues to a maximum of two weeks. Then the first "erythema" of the normal tissues appears, followed by ulceration and sclerosis if the dosage is large, while recession of the tumor stops and its regrowth is soon apparent. Damage to the tumor never continues beyond the beginning of damage of the normal tissues as signalized by "erythema."

II. Fractionated Irradiations of Sarcoma

Clinical treatment has been developed by trial and error, sometimes disastrous. It is astonishing that nobody has reported fractional irradiations of rat tumors for guidance of human therapy or for their intrinsic interest.

The necessary explorations of a wide range of dosages and intervals can be compressed in the following summary. Sittenfield's idea[7] of a small dose to sensitize to later higher dosage is particularly inapplicable to these rapidly growing tumors, which soon become hopelessly large if the initial dose is less than 1,000 or preferably 1,500 r. The reverse plan is much better, namely about 3,500 r to check the tumor radically, and small later doses to extend the control. Repetitions even of small doses as often as thrice weekly are inadvisable because the effect is too much like that of a single large dose. In general, it has been

best to wait ten to fourteen days until the effect of the initial large dose is wearing off, then follow with doses of 1,000 or 500 r a week or two apart. The legs have not tolerated more than 4,000 or 4,500 r total. Some animals have been enabled to live one or two months beyond controls, but the most marked recessions have never reached the point of cure.

Comments on Sections I and II.

1. The transplantable rat tumors furnish a useful reproduction of radioresistant human tumors, being subject to various degrees of recession with doses which the normal tissues can tolerate, though never curable.

2. The benefits of irradiation, in retarding growth, reducing tumor size and prolonging life are better obtained with fractionated than with single treatments, though the total dosage is not greatly different.

3. Whole body irradiation, radiation sickness, and action on sensitive normal structures such as lymphoid tissue resemble the action on tumors in the absence or brevity of a latent period. Particularly striking is the end of tumor recession when the visible reaction of normal tissues begins. It is uncertain whether such a distinction prevails between peripheral tissues and viscera, tumors then belonging with the latter as parenchymatous structures. Though the limit is less precise than in the rat, human tumors are evidently cured only within an early period after irradiation; for even if growth is retarded by fibrosis and impaired nutrition in the degenerative stage, nobody expects cure of a tumor at any very long time after the last radiation treatment.

C. ROENTGEN RAY AND TEMPERATURE ELEVATION

Heat may be considered as acting directly on tissues or as modifying the effects of radiation. Tumor cells are more sensitive to heat than mature tissues, but in comparison with young growing normal cells the difference is slight or doubtful.[8] Augmentation of the effect of radiation is accepted on three grounds, namely the temperature itself, increased oxygenation, or simple increase of local blood content regardless of oxygenation.[9] Besides references cited in the preceding paper and to be cited on irritants and temperature, the existing status may be generalized as follows.

1. Increased temperature and other causes of hyperemia or inflammation have been shown to augment the reaction to radiation, but no curative virtue in the sense of a specific difference of reaction of neoplasms and normal tissues has been accepted in clinical practice. The report by Shoulders *et al.*[10] of increased effectiveness of radiotherapy when given during fever produced by a hot cabinet has not been followed up by these writers or others. On the contrary, heat and other inflammatory agents are avoided as dangerous, systemic fever and local inflammation being generally held as contraindications to irradiation.

2. The entire literature on increase of radiation effects by heat has pertained only to the early erythema stage. It could, therefore, have practical interest only in the pioneer period of single massive treatments limited by the inflammatory reaction. Today, when the limitation is not any early inflammatory danger but only the late degenerations from total dosage, any benefit of heat must be in a form not touched upon by previous writers; that is, it must decisively increase the sensitivity of tumors in comparison with normal tissues in the early stage when cure is possible, or it must reduce the lasting damage to normal tissues so that they can tolerate higher total dosage without degeneration. If smaller fractionated doses with heat have a specific effect equal to that of larger doses without heat, better curative action is to be anticipated within the limit of tolerated total dosage. The preceding paper failed to show whether this total tolerance limit is changed by cold, and the question is open as regards heat. Is this tissue tolerance governed solely by

total radiation dosage, as now taught, or is it subject to modification by other physical agencies, particularly temperature?

3. Wood's assertion concerning the similar destruction of tumors by roentgen rays and heat, quoted at the outset of this paper, was based chiefly on the experiments of Rohdenburg and Prime[11] in his laboratory. Selective breakdown of large rat tumors in comparison with the surrounding normal tissues, and equal to the effects of much higher roentgen-ray dosage, was demonstrated with moderate radiation doses combined with long-wave diathermy. During the long time since the publication of this work, nobody has pointed out that the rats were all killed within two weeks or less; in other words, within the latent period before the reaction in the normal tissues was due to begin, even if it should be severe enough for total destruction. Ignorance of this elementary fact in the Crocker laboratory invalidated this supposed evidence of specific killing of tumors in comparison with normal tissues.

I. Roentgen Irradiation of Normal Tissues with Fever

Rats were made febrile by being laid for about ten minutes on ordinary hot water bags covered with cloths. Then during irradiation on the bags the fever could be maintained with little or no cover. No significant differences due to backscatter were noticeable. As individual temperatures were not thus kept equal, judgments were based on individual colon temperatures before and after treatment. There were some deaths from accidental hyperthemia. Temperatures were ordinarily kept between 105° and 108°F. A rise to 110°F. is fatal if continued for only a few minutes.

Whole Body Irradiation. The higher the fever, the greater is the radiosensitization. With the highest temperatures, rats died in six to eight days after as little as 500 r to the entire body. The suitable brief experiments must be distinguished from others in which rats are hot and sweating for a considerable time before irradiation, when they are killed by low dosage because of simple debility. At body temperatures approximating 106°F. rats were not killed by 500 r but were killed by two or three spaced repetitions, as compared with the previously described doses of 1,000 r at normal temperature. Pneumonia was the only common finding at autopsy, and the nature of the sensitization is again obscure.

Liver. Tolerance was observed for as much as eight doses of 500 r each, at body temperature 105–106°F., distributed during forty-one days, death occurring from pneumonia without cachexia. In general, an increase of liver sensitivity with fever was not evident.

Intestine. Heat evidently increased the injury of radiation limited to the intestinal region. Cachectic death resulted from four doses of 500 r with fever during three weeks, in contrast to the survival previously described at normal temperature.

Pelvis. Omitting lengthy details, increase of radiation injury by fever was shown by increased testicular atrophy and obvious lesions of the lower intestine.

Tails. As tails show earlier and sharper changes than legs, experiments on sensitiveness of peripheral tissues were limited to them. Besides the usual fever, the tails rested on the hot water bags so that their temperatures sometimes exceeded that of the body. The effect of single irradiations was both augmented and accelerated, "erythema" sometimes beginning as early as the eighth day, and extreme sclerosis or mummification resulting from doses of 2,500–3,000 r. No such augmentation was found with fractionated treatments. For example, six doses of 600 or even 750 r in the course of six months appeared harmless, as described at normal temperature. The possibility of an increase of tolerance was not tested.

II. Sarcoma Irradiations with Fever

Tail Tumors. Single and fractionated treatments in a varied range of dosage yielded no cures. Within the tolerance limit of the normal tissues, there may be marked

recession of the tumor but the tail separates at the tumor site leaving sarcoma in the stump. There seemed to be some suggestions of possibly better results by using very superficial tumors which were most accessible to heat beyond the febrile range, and which did not involve the main vessels of the tail.

Leg Tumors. Again disregarding fatal accidents, 15 rats gave the following results, all with fractionated treatments. Doses of 250 r were ineffective. Doses of 500 r, single or repeated, retarded growth about as much as 1,000 r at normal temperature. Four doses of 750 r in seventeen days, or four of 1,000 r during twenty-six days, caused shrinkage of some large tumors to small ulcers, but neither these nor any other combinations of dosage could prevent final recurrence. It could be clearly concluded that fever increases the specific radiation injury of tumors in comparison with normal tissues, though this does not reach the point of cure.

III. Sarcoma Irradiations with Local Heat

Attempts to destroy tumors by immersion in water at elevated temperatures had been disappointing,[1(o)] and that method was not suited for simultaneous irradiation. Therefore, a dry oven was improvised, heated with an ordinary electric bulb and having a small annex only 5 cm. wide, roofed first with cardboard and later with transparent plastic. Rats' legs could be inserted through holes in the sides, or tails could be inserted with their ends protruding through holes in the opposite side in order to spare the tips which are more vulnerable than the main part. Irradiation could thus be given through the cardboard or plastic roof while heating was in progress. The fault of the equipment was in the lack of fixed temperature control.

All tail tumors available at the time were used up in trials which, though somewhat encouraging, were spoiled sooner or later by accidents with the new apparatus. Tails are especially liable to overheating.

Numerous deaths from ulceration of large leg sarcomas left only eight significant trials with this class. Fractionated treatments were given, approximating the quantity and spacing in the above-described experiments with fever. Oven temperatures ranged between 140° and 190°F., the higher levels being tolerated only for shorter periods. Feet had to be shielded. Thermocouple measurements showed that the tumors were heated chiefly on the surface and (contrary to conditions in tails) the temperature in the depth of a large tumor approximated that of the body, which commonly rose to 103° or 104°F. during a treatment. The superficial portions sloughed with comparatively small roentgen-ray doses. Some survivors showed distinct increase of longevity, apparently aided by a drying effect of heat on the ulcers. There were no cures or permanent survivals except after loss of the entire leg.

IV. Ultrasound for Sarcoma

Some early reports in the literature suggested a possibility that ultrasound might produce the type of inflammation which would be conducive to the destruction of tumors. An unpublished investigation, in collaboration with Drs. F. K. Safford and J. R. Lisa, proved negative as regards curative action on tumors with the pulsating current or any interrupted treatments which prevented severe heating. Subsequently I tried ultrasound for heating, and arrived at the following experiments on 2 rats.

An incision below the tumor was used for extruding the necrotic center, and two days later for inserting a slender thermometer. The tumor leg and adjacent parts were immersed in water at room temperature to receive under-water treatment, while the forepart of the body was surrounded with crushed ice. Under nembutal, the colon temperature at the outset was 97°F. and the tumor temperature 94°F. Ultrasound was given for fifteen minutes, at No. 4 Permanent on the machine and distance from sound-head to tumor 1 inch. The

tumor temperature was thus raised to 110°F. while, by reason of the ice, the colon temperature was never above 104°F. The resulting tense, hard swelling of the tumor without a skin burn was of special interest, as the type of inflammatory reaction which has appeared significant for its effect on local circulation and metabolism.[12] This type is unusual in the rat, except after suitable ligations. It has been sought vainly with a variety of injections and other measures, including the previously mentioned heating in water,[1(o)] all of which produced the usual soft flabby edema, often with bright hyperemia.

Therefore, on the following day this treatment was followed up with irradiation of 2,500 r. The sloughing which ensued included not only tumor but also bone, the special heating of bone with ultra sound being familiar. One leg was finally lost by slow ulceration; the other healed with deformity from loss of bone, but both rats lived permanently tumor-free. This result clarified the problem by bringing it back to the point which was dominant throughout the research on ligation, namely the right kind and degree of inflammation. Ultrasound has disadvantages, at least in the rat. Therefore, other sources of heat were tested from this standpoint.

V. Inflammation and Irradiation of Normal Extremities

With the same improvised oven, trials of critical temperatures were made which were not feasible during irradiation. Though handicapped by the lack of fixed temperature control, it could be shown that the tail is destroyed by oven temperatures of 200–210°F. for five to ten minutes, and the reason is revealed by thermocouple readings up to 125°F. inside the tail. The leg under the same conditions has subcutaneous temperatures no higher than 110° F. and much lower in the muscles. Some crude reciprocal relations of time and temperature could be established. The tail may tolerate 140–150°F. for thirty minutes but not 130–140°F. for sixty minutes. Also 160–180°F. may be safe for fifteen to twenty minutes but not always for thirty minutes. Unfortunately, lack of equipment prevented any accurate contribution toward filling the existing void of knowledge concerning tissue tolerance for various combinations of temperature and time.

The effect of repetitions of heating is another unexplored problem. It could only be established that repetitions appear harmless if there has been time for complete recovery from the previous heating. But if there is a persisting effect, even to the extent of a very slight redness, a very moderate degree of heat can be extraordinarily destructive. These cautions must be emphasized if human tissues are heated to critical temperatures.

Observations with addition of radiation merely confirmed the familiar sensitizing influence of inflammation. After a thermal burn which in itself would not be dangerous, radiation doses which alone would not be dangerous can be destructive if given either immediately or in the course of days while inflammation is in progress. Thus, the mildly burned leg or tail of a rat can be destroyed by as little as 1,000 r of roentgen rays. The latent period is shortened to a less degree, but both the acceleration and the destruction are in proportion to the inflammation.

The main principle to be deduced is that time and temperature of heating are only means to an end. Various combinations can produce equivalent effects. Fair results can be obtained by judging empirically the degree of inflammation. It is unnecessary that the heat for this purpose should be applied during the irradiation.

VI. Inflammation and Irradiation of Sarcoma

Oven heat of the degrees now considered produces earlier and different changes in the tumor than in the normal tissues. In the leg, the congestive swelling of the tumor is evident. It acquires more or less of a bluish tinge, in contrast with the bright arterial hyperemia of the normal environ-

ment. Ulcers or incisions in the tumor ooze dark venous blood. These effects resemble those of ligation. Such changes are less plain in the tail with its thick skin and scantier circulation; but with certain degrees of heat a water-clear fluid exudes through the seemingly intact skin over the tumor and not elsewhere. This transudate may be comparable with the blister fluid which was found tumoricidal by Lohmann.[14]

Leg Tumors. A series comprising a wide variety of temperatures, times and radiation doses failed to furnish any cures of the usual large sarcomas. Even when trimming or curetting reduces them to flat ulcers, there are always cells deep amid muscles where heat does not penetrate effectively. Recessions and gain in longevity were often better than had been obtainable with heat alone or radiation alone.

Cures were obtained only in 2 specially prepared rats, with very superficially implanted tumors, two to three weeks old and smaller than usual, 1.6 or 1.8 cm. in diameter, and with the overlying skin excised for free exposure. In one instance heat of 160–170°F. was given for fifteen minutes on three successive days, and radiation of 2,500 r on the following day. In the other case, heat was given on one day, 1,500 r of radiation the next, and heat again on the day after. The permanent cures with these relatively small radiation doses were unaccompanied by any lasting injury of normal parts.

Radiant Heat. Because of the known poor penetration, superficial tumors treated with an infrared lamp were first denuded of skin. Daily repetitions of such treatments to the limit of tolerance failed to cure with heat alone, though the ulcers left by superficial sloughing were very shallow. After repetitions of the heat on four or five successive days, 2 rats were permanently cured by radiation of 1,250 and 1,500 r respectively.

Tail Tumors. The ease of through-and-through heating of the tail recommends it for dry oven treatments. Omitting accidental terminations, there were completed observations on 19 tail tumors, all four to six weeks old and 2 to 5 cm. long. The heating ranged between 140 and 200°F., and times of ten to forty minutes, most often fifteen to twenty minutes. Radiation was given either one or two days after the heat, and when necessary was followed by further heat treatments. Doses of 750 r being ineffectual, the individual irradiations were of 1,000, 1,250 or 1,500 r. Heat effects being judged chiefly empirically by the inflammatory appearances, as mentioned, it was shown that higher radiation could supplement lower heat, and vice versa. The cures were specific in the sense of leaving the normal tissues unharmed, so that separation of the tail at the tumor site occurred in only 3 instances, even with large tumors which penetrated to the main vessels, and ordinarily there was healing with normal scar formation. Also the cures were dependable, because the heating could be harmlessly repeated at appropriate intervals and the radiation doses were low enough to permit of repetition. Thus, for the first time it became possible to approach these tumors with confidence of a cure, except for the danger of burns due to lack of fixed temperature control. In 1 instance the cure was effected without interruption of an existing pregnancy. Cures were missed when the heat treatments and the irradiations were given too many days apart. There was no observed difference according to which treatment was given first.

VII. Sarcoma Treatment with Heat Alone

At this point it seemed desirable to turn back for tests of more intensive heat than had been given simultaneously with irradiation (Section III). The necessary penetration was feasible only with tail tumors. In treatments of 15 large tumors with combinations of time and temperature as near as possible to the tolerance limits of normal tissues, the results were either failure to cure or destruction of the tail by overheating. There were cures of 3 other tumors

which were superficial, about four weeks old and 1 to 1.8 cm. long. The successful treatments consisted of: (a) fifteen minutes at 170–180°F. on two successive days; (b) one treatment at 165–175°F. for twenty-five minutes; (c) thirty minutes at 170–180°F. resulting in recession to small shallow ulcer, with recurrence after one month treated fifteen minutes at 165–175°F., and persistence in the ulcer floor eighteen days later finally cured by twenty minutes at 180°F.

It is thus confirmed that there are critical temperatures at which tumors can be destroyed by reason of their less tolerance of heat as compared with normal peripheral tissues. The cures are more difficult than with the aid of radiation, and are possible only for superficial tumors. The determination of the critical temperatures would be possible only with accurate apparatus.

VIII. Diathermy and Roentgen Irradiation for Sarcoma

Besides the previously mentioned work of Rohdenburg and Prime,[11] specifications for the cure of rat or mouse tumors by roentgen irradiation combined with diathermy have been given by Fuke[12] for long wave and Sugiura[6] for ultrashort wave. This knowledge, like the above-described experiments with oven heat, remains theoretical and no practical application has ever been attempted, for the reason that the method is applicable only to small animals. Though diathermic heat theoretically penetrates, as the name signifies, the actual effect of the available methods in man or any large animals is to burn the skin and superficial tissues before producing any approach to a critical temperature in any deep structures. Furthermore, the efficiency of the blood circulation in distributing heat not only opposes the deep heating but also gives rise to systemic fever if any large tissue mass is greatly heated. Because of these circumstances, there has never been even an attempt to learn the time-and-temperature tolerance of any deep organs.

For the present purpose, the need is for a method which can be tested in small animals and yet has possibilities of use in some locations in large animals or man. A beginning has been made by an adaptation of the writer's previous work on refrigeration. Diathermy, being not heat but electromagnetic energy, can be projected through a zone of cold. Thus, by chilling the skin and other superficial tissues to a desired degree and depth, it is easily possible to have deep temperatures higher than superficial temperatures. Tendencies to systemic fever can be counteracted by cooling other parts of the body. This method was developed in collaboration with Dr. F. K. Safford and it is hoped that it will be published in a separate paper.[1p]

For the rat tumor experiments it has been convenient to use the "Raytheon" apparatus, furnishing so-called microwaves of about 12.5 cm. length, which produce rapid heating with marked skin-burning tendency and thus test the control method. This consisted ordinarily in spraying the skin with ice water during the diathermy treatment. To emphasize penetration, the treatment was used entirely for large leg tumors for which ordinary heat had failed. After trials, attempts to cure such tumors by diathermy alone were abandoned, for though theoretically feasible such a cure requires critical temperatures which in practice cannot be maintained uniformly throughout any considerable tissue mass.

Preliminary trials which included fatal burns in 17 rats provided sufficient working rules for normal legs. Tumors presented an additional problem because of the greater bulk of the leg and the easier tendency to necrosis. Several methods, besides the thermocouple, for estimating tissue temperatures at various depths need not be detailed. Diathermy treatments were for ten to twenty minutes, usually fifteen minutes. Subcutaneous and colon temperatures were easily kept below 100°F. Tumor temperatures of about 110°F. were preferred, 112°F. being tolerated but 115°F. for any considerable time being destructive. Body temperatures were further controlled by shield-

ing and by spraying if necessary. Roentgen-ray doses of 1,000 r were inadequate. Doses of 1,500, 1,750 or 2,000 r were sufficient according to the degree of heating, and it was immaterial whether they were given a day before or a day after the diathermy. Since repetitions of the heat were harmless after suitable intervals, the moderate roentgen-ray dosage left leeway for further treatments if needed.

Attempts to treat leg tumors 4 to 6 cm. in diameter were over-ambitious, the large ulcerations causing loss of leg or life in 21 rats. Using tumors 2 or 3 cm. in diameter, success was practically assured if purely accidental burns were avoided. With such tumors the ulceration and intoxication were much less than under previously described treatments. Thus 16 rats met the test of permanent tumor-free survival, and for the first time there could be confidence toward them similar to what was felt toward the tail tumors with oven heating.

Examples of the roentgen-ray dosage are: (a) cure by single dose of 2,000 r; (b) recurrence after 2,000 r, cure by 1,000 r two weeks later; (c) a case, heretofore utterly hopeless, of leg sarcoma 2.5 by 2 cm., tail tumor 4 cm. long, and tail tumor metastasis on the rump 3 cm. in diameter. The leg and rump tumors were given fifteen minute microwave treatments with radiation of 1,750 r. The tail tumor regressed considerably with five oven treatments three days apart. One day later the tail was given its single irradiation of 1,750 r. After another day the combination of microwave and 1,750 r to the tail and rump was repeated. It was exceptional not only that the multiple tumors were cured but the body weight of 240 gm. never fell below 190 gm.

DISCUSSION

The extensive or complete breakdown of malignant tumors through an inflammatory reaction excited by temporary ligation, without the intervention of any outside agent, was the starting point of this research. The phenomenon seemed important enough to warrant continued efforts for the past twenty years, notwithstanding the negative attitude of all the large cancer institutions. During this time other methods of producing inflammation have failed to cause the same hard swelling as ligation, and have likewise failed therapeutically. Most of the chemotherapeutic agents proposed in the literature have failed to show adjuvant value in connection with ligation. The inflammatory theory and its practical applications have been set forth in several papers, particularly the most recent one.[1k] Under the plan of choosing the most resistant animal tumors and the most difficult conditions, the experimental cures have been few but they have reversed the previously universal experience, for instead of favorable experimental results which fail in clinical application, the human tumors which are accessible to ligation have been more easily and markedly affected than the tumors of rodents.

The resemblance of the inflammatory reaction produced by certain modalities of heat to that produced by ligation led to a successful treatment of these resistant rat tumors. This is not only an escape from the limitations imposed by ligation; it also gives better curative results alone and especially in combination with roentgen irradiation. The problem is not merely one of critical temperatures which may kill normal or tumor cells in vitro. The predominance of the inflammatory factor in vivo seemingly accounts for the equivalent effects obtainable with a rather wide variety of time and temperature combinations. Heat may be considered from two standpoints: (1) by itself, (2) as an adjuvant to radiation.

(1) Heat (or the inflammatory reaction to heat, ligation, etc.) may rank as the most positive and specific antitumor agent, because: (a) it destroys all kinds of neoplasms indiscriminately, none being resistant; (b) it can be repeated at suitable intervals indefinitely, without any apparently cumulative effect; (c) tumors never acquire resistance with such repetitions, but may rather under some conditions became sensi-

tized to easier killing. Thus, while the development of radiotherapy has been in the direction of constantly greater frequencies and smaller wavelengths, it is of interest that the most specific tumor-killing action lies toward the opposite end of the energy spectrum.*

(2) Because of the practical obstacles to these theoretical possibilities, it is fortunate that heat is adjuvant or synergistic with roentgen rays. As already mentioned, the previous literature on the augmentation of roentgen-ray effects by heat or inflammation has pertained only to the early erythema stage, and there has not been a single investigation of the only point of practical importance, namely the influence on late degenerative processes. There is still a need for precise determination whether these late results of fractionated treatments are governed solely by total dosage, or whether they can be modified by heat or cold. This problem is separate from roentgen-ray "burns," which are known to be modifiable. It concerns especially the cumulative effects of spaced irradiations in doses which never cause an erythema. The present work at least has given no indication of a reduction of the total roentgen-ray tolerance of normal peripheral tissues by the concomitant elevation of temperature. The important practical point, then, is the increased tumor-killing potency of doses within the tolerance limit.

The foregoing experiments dealt only with the so-called peripheral tissues, not with parenchymatous organs. Obviously, the great majority of tumors which occur in viscera offer the greatest difficulty, because of their relative inaccessibility and their varying resistance. There are differences in the radiosensitivity of different organs and of the tumors arising from them. Different viscera also differ in their tolerance of asphyxia, and the ligation treatment of tumors in them was not altogether discouraging.[1h] Differences in the reaction to heat may likewise be anticipated, and the requirements are, first, to learn the respective tolerance limits and, second, to develop apparatus to deliver heat as needed. Mere febrile temperatures, or the nominal diathermy which is customary among physical therapists, must be replaced by temperatures near the tolerance limits for important effects in cancer and perhaps some other pathological conditions. The delivery of temperatures of the requisite degree and localization may not be beyond hope, if as much energy and ingenuity are employed as have been devoted to perfecting roentgen-ray apparatus. It is necessary to establish the clear fact that tumors, even of the radioresistant type, can be definitely destroyed by what may be called a cross-fire of long and short energy waves. Practical therapy then becomes an engineering problem which should not be beyond solution.

* This is apart from the dispute over "hard" and "soft" roentgen rays. The action of heat is entirely different. "Thermal deaths due to raised temperature would take 10,000 times as much absorbed energy as radiation deaths."[13] It may be remarked, however, that the prevailing theory of roentgen-ray effects governed solely by the amount of absorbed energy must depend on concrete proof. The minority who still cling to qualitative differences between roentgen rays can hold that the seemingly attractive unitarian theory is logically implausible. They might compare it to an assertion in mechanics that mass and velocity are immaterial if total energy is the same. Also, throughout the entire energy spectrum different wavelengths produce markedly different effects, and it may be inquired why these differences should vanish just in the roentgen-ray band.

SUMMARY AND CONCLUSIONS

1. The effects of whole body irradiation are quickly evident, but no local effects on legs or tails are grossly perceptible until after a fixed interval of about two weeks, even if the dose has been high enough for total destruction. The rapidity of physiological processes in the rat is the basis for a question whether the changes seen after this long interval correspond to the human erythema, or the later degenerative stage, or both.

2. As anticipated, considerably higher total radiation is tolerated in the form of suitably spaced fractional doses than in single doses, to either the whole body or local parts. But the repeated whole body irradiations have a sensitizing action of unknown nature, in that the rat retaining apparently vigorous health is finally killed

acutely by a small dose.

3. Tumors were implanted in convenient leg or tail locations. The radioresistance of the rat sarcoma was confirmed, in that it withstands higher radiation than is ever given in single doses to human tumors. The first trials of fractionated radiation have been made, and show that the tumor is incurable by any quantities or timing of doses that could be devised. The recessions, however, are evident and sometimes great, so that the tumors are well suited for therapeutic tests.

4. Interesting time relations have not been mentioned in previous literature. The tumor recession begins promptly, like the effect of radiation on the whole body, or on sensitive structures such as lymphatic tissue or bone marrow. This tumor recession is ended some time during the latent period of the surrounding peripheral tissues, and there is never any further tumor recession after the visible reaction of the normal tissues has begun. A comparison with the time relations in human treatment is suggested.

5. Existing literature gives abundant examples of increase of radiosensitivity by irritation, inflammation or hyperemia, but the two vital points are lacking. (a) It is not shown whether this augmentation affects predominantly tumor or normal tissues. (b) The reports pertain only to the primary erythema and ignore any influence on late degenerations, which are the actual limiting factor in modern radiotherapy. The present observations began with experiments showing that fever increases sensitivity to whole body irradiation and to single large irradiations of tails, but not to smaller fractionated irradiations of tails.

6. Therapeutic experiments with fever gave encouraging indications of selective increase of radiosensitivity in tumors, but deaths due to intoxication from large necrotic masses left the results inconclusive.

7. The results of local heat during administration of roentgen rays were somewhat similar, but failed to indicate that the mere temperature at the time of irradiation was very decisive.

8. Ultrasound failed to produce an inflammatory or other curative action until it was used to produce local heat. Then the tense hard tissue swelling and the accompanying effect on tumors gave a clue for further procedures, in line with previous ligation experiences.

9. Inflammation by dry oven heat which could penetrate through-and-through tail tumors made them definitely curable by moderate roentgen-ray dosage which was otherwise ineffectual. Cures of leg tumors, with either oven heat or infrared, were limited to a few which were sufficiently small and superficial to permit adequate elevation of temperature throughout.

10. Tail tumors were proved capable of cure by heat alone, but the treatment must be more severe and the temperature nearer to the tolerance limit of normal tissues than when roentgen radiation is added. To some extent such cures perhaps represent direct killing due to lower heat tolerance of tumors than of mature normal peripheral tissues, but a secondary inflammatory reaction is believed to be predominant.

11. A method of microwave diathermy with refrigeration of the skin was used to produce deep heating without burns of superficial tissues. Decisive cures of large leg tumors were thus obtained in combination with roentgen-ray doses which were within safe limits for the normal tissues. The effects of these two forms of energy may be not merely additive but synergistic.

12. The following are reasons why heat is the most specific and decisive physical agent for killing tumors: It can destroy all tumors, including the radioresistant. Resistance to it is not acquired. Treatments can be repeated indefinitely, because if burns are avoided there are no cumulative or degenerative consequences.

It is suggested that improved apparatus be developed for the therapeutic realization of these theoretical possibilities in combination with roentgen radiation.

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Thirty-eighth Annual Meeting: 1956, to be announced.

EDITORIALS

RADIATION INJURY OF THE CENTRAL NERVOUS SYSTEM

OVER the years a voluminous literature has accumulated on the effects of penetrating radiations, particularly roentgen rays, of various energies on the central nervous system. As a result of many experimental investigations in different animal species and numerous clinical observations in man, two conclusions seem to have gained the greatest popularity: first, that the central nervous system is very radioresistant, and second, that if a demonstrable effect is produced upon it by irradiation, this usually is associated with relatively severe vascular changes, suggesting that the primary injury lies in the vascular system.

During the past decade several reports have appeared casting some doubt on the validity of these conclusions.

In 1945, Wachowski and Chenault[1] made an exhaustive review of the salient articles published up to that time. These authors observed six patients with intracranial tumors in whom definite signs and symptoms of brain damage developed following administration of large doses of 200 kv. roentgen therapy and wished to correlate their observations with those of other investigators. Because of the assumed high radioresistance of the nervous system there was a tendency at that time to deliver doses to intracranial tumors which were definitely larger than those given to malignant neoplasms in other locations of the body and this procedure was amply supported in the literature. The tumor doses in the six cases of Wachowski and Chenault ranged from 6,150 roentgens in thirty-two days to 8,910 roentgens in eighty-four days. Three of the six patients came to autopsy and showed extensive degenerative changes in the cerebral tissue, one of them having received a dose that was repeatedly quoted by other investigators as being safe for brain tissue. The most interesting finding, however, was that "the striking damage to the nerve tissue did not have a counterpart in the vascular structures."

Recently, Arnold and his co-workers[2,3,4,5] published an excellent series of observations on the effects of roentgen irradiation on the primate brain, employing the 23 mev. medical betatron at the University of Illinois. They used adult monkeys (*Macaca mulatta*) as an experimental animal and also extended their observations to humans. This work effectively dispels the belief that the components of the central nervous system are highly radioresistant and that irradiative phenomena in these tissues are principally secondary to vascular changes. It is postulated[4] that these erroneous impressions were the result of studies made after the brain had "recovered" and returned to histologic normality.

Arnold, Bailey and Harvey[3] have shown the brain stem and hypothalamus to be more radioresponsive than the cortical tissue. This selectivity is not readily ex-

[1] Wachowski, T. J., and Chenault, Harvey. Degenerative effects of large doses of roentgen rays on the human brain. *Radiology*, 1945, *45*, 227–246.

[2] Arnold, A. Effects of X-irradiation on the hypothalamus: A possible explanation for the therapeutic benefits following X-irradiation of the hypophyseal region for pituitary dysfunction. *J. Clin. Endocrinol. & Metabol.*, 1954, *14*, 859–868.

[3] Arnold, A., Bailey, P., and Harvey, R. A. Intolerance of the primate brainstem and hypothalamus to conventional and high energy radiations. *Neurology*, 1954, *4*, 575–585.

[4] Arnold, A., Bailey, P., Harvey, R. A., Haas, L. L., and Laughlin, J. S. Changes in the central nervous system following irradiation with 23-mev. X-rays from the betatron. *Radiology*, 1954, *62*, 37–44.

[5] Arnold, A., Bailey, P., and Laughlin, J. S. Effects of betatron radiation on the brains of primates. *Neurology*, 1954, *4*, 165–178.

plained but is of extreme importance in view of the subservient function served by these areas. The easily identifiable cellular aggregates in the hypothalamus known as the paraventricular and supraoptic nuclei undergo marked histological alterations after rather moderate doses of radiation.[2,3,4,5] These microscopic findings consisting of a numerical deficiency and degenerative changes in the surviving cells are most evident usually after a period of a few months. Arnold[2] suggests these effects as an explanation for the clinical results of pituitary irradiation, particularly since it is quite impossible to irradiate the hypophysis without including the ventral portion of the hypothalamus.

In addition to the hypothalamic changes a selective destruction of the white matter occurs,[4] characterized by demyelinization initially and followed by actual necrosis of the myelin sheath, glial cells, and the axons. This is a destruction of the myelin and axons directly as is evidenced by its appearance prior to any sign of vascular obstruction.

The experimental results presented by Reynolds[6] in the Pancoast Lecture of 1942 are very illuminating in this respect. Reynolds, with his co-workers at Harper Hospital, Detroit, in studying the effect of 550 kv. roentgen rays on brain tissue, found that by making use of the polarizing microscope it is possible to demonstrate early myelin changes which cannot be shown by the conventional microscope. The myelin contains large amounts of lecithin which is a highly polar lipoid. A single dose of 1,200 roentgens of 550 kv. roentgen rays given through a port 0.5 cm. in diameter so impairs the optical activity of the lecithin that the damaged myelinated fibers of the brain of dogs can readily be visualized under the polarizing microscope. Similar observations were made in the normal portions of the brain in patients with brain tumors who were treated with 550 kv. roentgen rays and who died at various intervals thereafter due to their illness. It is not clear from these experiments whether the loss of the optical activity of the myelin below a certain dosage level constitutes a reversible process or is the forerunner of permanent damage. There can be no doubt, however, that it is a manifestation of the direct effect of the roentgen rays rather than of secondary vascular alterations.

Arnold and his co-workers[4,5] observed a distinct dose level relationship to the degree of damage produced in the brain. Monkeys receiving a single exposure of 7,000 roentgens were effectively lobotomized. Those receiving 5,000 to 7,000 roentgens died within a period of ten days to two weeks and exhibited extensive nonselective necrosis throughout the path of the beam. Those which received doses of 3,000 to 5,000 roentgens suffered acute reactions marked by neurological changes. These signs cleared in a few weeks, followed by complete functional recovery. Microscopic studies performed then revealed no histologic abnormality and it is suggested that previous misconceptions probably arose from examination of specimens prepared at this stage of the irradiation reaction. Monkeys in the last group which were given 3,000 to 5,000 roentgens were functionally unimpaired following subsidence of the acute signs until six to eight months after the irradiation. They then developed a delayed radionecrosis. It is stressed that 23 mev. roentgen rays produce only 8.5 ion pairs per micron of pathway in tissue, compared with 80 ion pairs per unit length of travel for conventional (200–400 kv.) roentgen rays. Although the intensity of ionization at these energy levels varies by approximately ten times, the effectiveness of the lower energy beams biologically is only 40 per cent greater, giving a conversion factor of 0.60, which was used to determine the equated dosages with the two types of radiations.

The appearance of delayed radionecrosis coupled with late hypothalamic nuclear

[6] Reynolds, L. Newer investigations of radiation effects and their clinical applications: Pancoast Lecture. Am. J. Roentgenol. & Rad. Therapy, 1946, *55*, 135–152.

alterations serves to modify our concepts of tolerated tissue doses in the central nervous system. Similar changes have been noted in humans following comparable dosages.[3]

These observations are highly significant since it appears that brain stem tolerance becomes an important controlling factor in roentgen therapy of brain tumors. They also help to explain the increasingly frequent reports during recent years of injury to the central nervous system, often fatal, following roentgen therapy of intracranial or extracranial lesions. Malamud, Boldrey, Welch and Fadell,[7] for example, collected twelve cases of cerebral necrosis, four cases of brain stem necrosis and three cases of spinal cord myelitis, all of which were confirmed by biopsy or postmortem examination. To these they added two cases of their own. Boden[8] likewise noted radiation injury of the brain stem and cervical cord in a considerable number of cases.

All in all, it may be said that our former concept of the very high radioresistance of the central nervous system is subject to certain modifications. Evidence is gradually accumulating that there is a direct effect of the radiation on nerve tissue similar to that observed on any other tissue included in the field of irradiation, although perhaps less definitively demonstrable in degree. The effect on the vascular system is similar, but because of the resulting impairment in the blood supply, it forms a delayed added cause of radiation injury to the central nervous system.

Kenneth L. Krabbenhoft, M.D.

[7] Malamud, N., Boldrey, E. B., Welch, W. K., and Fadell, E. J. Necrosis of brain and spinal cord following x-ray therapy. *J. Neurosurg.*, 1954, *11*, 353–362.

[8] Boden, G. Radiation myelitis of the cervical spinal cord. *Brit. J. Radiol.*, 1948, *21*, 464–469; also Boden, G. Radiation myelitis of the brain-stem. *J. Fac. Radiologists*, 1950, *2*, 79–94.

LEON J. MENVILLE
1882-1955

"The light he leaves behind him lies
Upon the paths of men."—Longfellow

IN THE death of Dr. Leon J. Menville on January 24, 1955, American radiology lost one of its most distinguished members and the South and New Orleans a beloved and outstanding citizen.

A native of Napoleonville, Louisiana, Dr. Menville received his undergraduate training at Louisiana State University and was graduated in medicine in 1904 from the Maryland Medical College. He began the practice of medicine with his father at Houma, Louisiana, and continued in general practice for thirteen years, thus laying a stable foundation for his future eminent

career as a radiologist. He was an incomparable raconteur and his tales of those early days in the Bayou country are unforgettable. Having become interested in radiology, he did graduate work in that field at the Mayo Clinic and in 1918 began the practice of his specialty in New Orleans.

Dr. Menville joined the medical faculty of Tulane University, New Orleans, in 1919 and later became Professor of Radiology in that institution, a position which he continued to fill until his retirement in 1948. He headed the Department of Radiology in Charity Hospital of Louisiana in New Orleans for ten years, and served also as radiologist at the Presbyterian, French, and Illinois Central Hospitals and as consultant at Hotel Dieu and Flint-Goodridge Hospitals in New Orleans, and the U. S. Veterans Hospital in Algiers, Louisiana.

Through his manifold activities, Dr. Menville became nationally, and indeed internationally, known as a radiologist. His confreres honored him with many citations and high offices during his long and illustrious career. He was a past president of the Louisiana State Medical Society and of the Louisiana State Board of Medical Examiners. He held membership in the State Radiological Society, American Roentgen Ray Society, American Radium Society, Radiological Society of North America, Southern Medical Association, and the Society for Experimental Biology and Medicine. He was a Fellow of the American Medical Association and an Emeritus Fellow of the American College of Radiology, a past chancellor of the American College of Radiology, and a member of the first American Board of Radiology. In 1953 the Radiological Society of North America elected him to honorary life membership, a distinction which had been conferred upon only eight other men. He was an honorary member of the Radiological Society of Cuba and a corresponding member of the National Academy of Medicine of Colombia.

In 1932, Dr. Menville received the Gold Medal of the Radiological Society of North America for his original work on the lymphatic system. He was also awarded the Gold Medal of the Louisiana Academy of Science for his achievements in the field of research.

Dr. Menville served with distinction for eleven years, from 1931 to 1941, as the Editor of *Radiology*, the official organ of the Radiological Society of North America. He guided the editorial policies of the journal with skill and finesse through the years of world economic instability. When he resigned as Editor to become President of the Society, he had the satisfaction of having brought *Radiology* to recognition as one of the outstanding radiological publications of the world. He served also on the editorial board of the *American Journal of Cancer* and the *New Orleans Medical and Surgical Journal*. He was the author of more than forty original medical articles and was a contributing author to several radiological textbooks.

During World War I, Dr. Menville served as First Lieutenant at Camp Stafford. He was a member of the Selective Service Board in World War II and held a commission as Lieutenant Commander in the United States Naval Reserve (Retired).

The above factual account lists some of the many accomplishments of Dr. Menville as a radiologist of international reputation. It does not, however, portray the respect and love felt for him by his many patients, friends, and colleagues. Kindness and gentleness, combined with firmness, when this was called for, were as much a part of his professional life as was his scientific acumen. It was the writer's privilege to be associated with Dr. Menville on the staff of *Radiology* for many years and to be the recipient of much wise counsel based on his experience and good judgment. Many associated with him in other aspects of his specialty will bear similar witness.

Dr. Menville is survived by his wife, the former Miss Marie Marmande, by two daughters, Mrs. Robert Dupont and Mrs. William M. Allin, and by a son, Dr. John G. Menville of New Orleans.

Howard P. Doub, M.D.

WILLIAM PATRICK HEALY
1876-1954

DEATH came rather suddenly to Dr. William Patrick Healy at his home, 1 East 66th Street, New York City, on November 7, 1954. Born in Bridgeport, Connecticut, on March 17, 1876, it was natural that he was affectionately known to his friends as "Pat." His early schooling was obtained at the local public schools. He graduated from Sheffield Scientific School, Yale University, in 1896 with honors, and from Johns Hopkins Medical School in 1900. His internship began at the New York City Hospital on Welfare Island where he served from 1900 until 1902. Internship on the Gynecological Service at the Roosevelt Hospital in 1902 was the

beginning of a life long association with that institution.

Dr. Healy's active professional appointments included Assistant Visiting Obstetrician at New York Lying-In Hospital 1903–1904; later Attending Obstetrician and Gynecologist 1945–1947; Assistant Visiting Surgeon at Knickerbocker Hospital 1908–1915; Visiting Gynecologist at Misericordia Hospital 1908–1920; Junior Visiting and later Assistant Gynecologist at Roosevelt Hospital 1910–1928; Visiting Surgeon at Fordham Hospital 1908–1921; Director of the Department of Gynecology at Memorial Hospital for the Treatment of Cancer and Allied Diseases 1922–1942. He was also a former Dean of the Medical School of Fordham University and later a Professor of Clinical Obstetrics and Gynecology at Cornell University Medical School. He was also a member of the Board of Appeals, Number 25, New York City Selective Service.

Honorary professional appointments included Consulting Gynecologist Emeritus to Memorial Center for Cancer and Allied Diseases; Consulting Gynecologist to Roosevelt Hospital; Caledonia Hospital, Brooklyn; Elizabeth A. Horton Memorial Hospital Middletown, New York; Misericordia Hospital; New York Infirmary for Women and Children; Polyclinic Hospital Tumor Clinic; St. Clare's Hospital; Northern Westchester Hospital, Mt. Kisco, New York; St. John's Riverside Hospital, Yonkers, New York; St. Joseph's Hospital, Yonkers, New York; St. Luke's Hospital, Newburgh, New York; Sea View Hospital, Staten Island; Monmouth Memorial Hospital, Long Branch, New Jersey; Fitkin Memorial Hospital, Neptune, New Jersey.

Dr. Healy was a Fellow of the American Medical Association and a member of the New York State and New York County Medical Societies (president of the New York County Medical Society in 1926). He was a Fellow of the American Gynecological Society (president 1952–1953); New York Obstetrical Society (president 1927–1928); the American College of Surgeons, and the American College of Radiology. He was also a member of the American Radium Society and president in 1938.

His gracious manner and pleasing personality combined with superior surgical skill and endless energy brought him well deserved national acclaim, but he attained international fame because of his work in the field of cancer of the female genitalia. He addressed international societies on this subject at Copenhagen and Madrid, as well as in this country. His recognized diagnostic acumen resulted in a large consulting practice.

Dr. Healy's contributions to medical literature were many and his interest in clinical research was at a constant high level. His chief interest, however, was in the patient as an individual rather than as a statistical factor, and he proved by his conduct he believed that by treating the patient he was most effectively treating the disease.

With the passing of this thorough gentleman, a great doctor and a fine friend to all who knew him, the radiological world has suffered a great loss but his accomplishments remain as a cherished memory for us and as a memorial to him.

He is survived by a devoted wife, three sisters, two daughters and one son. Their loss is shared by a host of admiring friends.

Frank R. Smith, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Palmer House, Chicago, Ill., Sept. 20–23, 1955.

American Radium Society
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: Shoreham Hotel, Washington, D. C., April 21–23, 1955.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: 1955, to be announced.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois. Annual meeting: 1956, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual Meeting, Atlantic City, N. J., June 6–10, 1955.

Eighth International Congress of Radiology
Secretary General, Dr. José Noriega, Calle del Oro 15, Mexico 7, D. F. Meets in Mexico City, Mexico, July 22–28, 1956.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. J. A. Norton, 843 Donaghey Bldg., Little Rock, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Radiological Society
Secretary, Dr. Daniel G. Butera, 709 E. 39th St., Brooklyn, N. Y. Meets first Thursday of each month October through April.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Clayton G. Weig, 135 Linwood Ave., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse, N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. E. Burns Lewis, 670 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. H. F. Inderlied, 11311 Shaker Blvd., Cleveland 4, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. S. A. Patterson, Larimer County Hospital, Fort Collins, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. B. B. Alicandri, 20 Maple St., Springfield, Mass. Meets second Friday October and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. A. H. Keene, 3707 Gaston Ave., Dallas, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, Oct. through May, at David Whitney House, 4421 Woodward Ave., at 6:30 P.M.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. J. T. Shelden, Box 1021, Lakeland, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Herbert M. Olnick, 417 Persons Bldg., Macon, Ga.

Greater Miami Radiological Society
Secretary, Dr. A. S. Capi, 300 N. 20th Ave., Hollywood, Fla. Meets monthly third Wednesday at 8 P.M. at various South Florida Hospitals.

Houston Radiological Society
Secretary, Dr. W. C. Owsley, 6409 Fannin, Houston 25, Texas. Meets fourth Monday each month at Texas Children's Hospital.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. John A. Robb, 238 Hume-Mansur Bldg., Indianapolis 4. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society, The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. A. M. Cherner, Hays, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. David Shapiro, 217 East Chestnut St., Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

* Secretaries of societies are requested to send timely information promptly to the Editor.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Oscar Harvey, 3741 Stocker St., Los Angeles 8, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. W. A. Russell, Augusta General Hospital, Augusta, Maine. Meets in June, October, December and April.

MARYLAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Paul W. Roman, 1810 Eutaw Place, Baltimore 17, Maryland.

MEMPHIS ROENTGEN SOCIETY
Secretary, Dr. B. E. Greenberg, 294 Annella St., Memphis 11, Tenn. Meets first Monday of each month at John Gaston Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. R. W. Byrne, 3321 N. Maryland Ave., Milwaukee 1, Wis. Meets monthly on fourth Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. James M. Packer, 621 High St., Jackson, Miss. Meets third Thursday of each month at Hotel Edwards, Jackson, at 6:00 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Meets at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Alan E. Baum, Hicksville, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Oamaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets third Friday of each month, October through May, at Hotel Commander, Cambridge, Mass.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Sidney Rubenfeld, 477 First Ave., New York 16, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Marianne Wallis, St. Joseph's Hospital, Minot, N. Dak. Meetings by announcement.

NORTH FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. Ivan Isaacs, 1645 San Marco Blvd., Jacksonville, Florida. Meets quarterly in March, June, September and December.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. M. M. Thompson, Jr., 319 Toledo Medical Bldg., Toledo 2, Ohio. Annual meeting, Mayflower Hotel, Akron, Ohio, May 20–22, 1955.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. F. C. Shipps, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Next annual meeting at Berkshire Hotel, Reading, Penna., May 20 and 21, 1955.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets second Wednesday of month, October through June at Hotel Roosevelt.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Paul W. Roman, 1810 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Wm. R. Dickens, Cincinnati General Hospital, Cincinnati 29, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. H. C. Chang, 1282 Emma St., Honolulu 13, T. H. Meets third Monday evening of each month at designated hospitals.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
Secretary, Dr. E. H. Stratemeier, Jr., 1010 Rialto Building, Kansas City 6, Mo. Meets last Friday of each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Carye-Belle Henle, 195 North 7th St., Newark, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital,

Augusta, Ga. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Henry H. Forsyth, Jr., 40 Meigs St., Rochester, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo. Mid-Summer Conference, Shirley-Savoy Hotel, Denver, Colo., Aug. 18–20, 1955.

St. Louis Society of Radiologists
Secretary, Dr. W. B. Seaman, 510 South Kingshighway, St. Louis 10, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas Meets Brooke Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
Secretary, Dr. J. C. Asher, 2001 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. T. M. Fullenlove, 110 El Verano Way, San Francisco 27, Calif. Meets quarterly at Grison's Steak House.

Section on Radiology, California Medical Association
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary, Dr. John A. Long, 1801 K St., N.W., Washington 6, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

South Bay Radiological Society
Secretary, Dr. H. R. Berman, 309 St. Claire Bldg., San Jose, Calif. Meets second Wednesday of each month.

South Carolina Radiological Society
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next Meeting, Fort Worth, Texas, Jan. 20–21, 1956.

Tri-State Radiological Society
Secretary, Dr. S. N. Tager, 219 Walnut St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Eva L. Gilbertson, 1317 Marion St., Seattle 4, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. M. G. Priestman, New Rochelle Hospital, New Rochelle, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. J. T. English, 2000 Van Ness Ave., San Francisco 9, Calif. Meets monthly, third Thursday at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico, Puerto Rico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiología, A. C.
Calle del Oro No. 15, Mexico 7, D. F.
Secretary General, Dr. Guillermo Santín, Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. Rafael A. Blanes, P. O. Box 9067, Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

Association of Radiologists of the Province of Quebec
Secretary, Dr. Jean-Louis Léger, 1560 Sherbrooke St., Montreal, Que. Meets four times a year.

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1

Faculty of Radiologists
Honorary Secretary, Dr. R. A. Kemp Harper, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicales
General Secretary, Dr. Ls Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151 Córdoba, Argentina. Meetings held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, JUNTA CENTRAL, BUENOS AIRES
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL LITORAL, SEDE, ROSARIO
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL SUR, SEDE, LA PLATA
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL CENTRO SEDE, CÓRDOBA
President, Prof. Dr. David L. Caro, Corro 86, Córdoba. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL NORTE, SEDE, TUCUMAN
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DE CUYO SEDE, MENDOZA.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6° piso, Bogota, Colombia. Meets last Thursday of each month.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary General, Dr. Amador Holgado V. Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

CONTINENTAL EUROPE

AUSTRIAN ROENTGEN SOCIETY
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

SOCIÉTÉ FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALE, and its branches: SOCIÉTÉ DU SUD-OUEST, DU LITTORAL MÉDITERRANÉEN, DU CENTRE ET DU LYONNAIS, DE L'OUEST, DE L'EST, ET D'ALGER ET D'AFRIQUE DU NORD
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX^e^, France.

CESKOSLOVENSK SPOLEČNOST PRO RËNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

DEUTSCHE RÖNTGEN-GESELLSCHAFT
Secretary, Dr. med. Peter Kröker, Evangelisches Krankenhaus, Huyssens Stiftung, (22a) Essen.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

NEDERLANDSE VERENIGING VOOR ELECTROLOGIE EN ROENTGENOLOGIE
Secretary, Dr. B. J. Rethmeier, Bornsestraat 378, Almelo, Netherlands.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. Juljusz Borejko, 59 Nowogrodzka St., Warsaw Poland.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

WROCLAW SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. R. Marciniak, Akad. Medyczna Wroclaw, 68 Curie-Sklodowska St., Wroclaw, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wroclaw.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S.I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ-SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

INDIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

In the future, the list of Meetings of Radiological Societies will appear in every other issue of the JOURNAL, that is, in 1955, in July, September and November.

DISTINGUISHED HONOR TO DR. CASE AND DR. DEL REGATO

The President of the Republic of Cuba, at the proposal of the Minister of Public Health, signed a decree awarding the National Order of Merit "Carlos J. Finlay" in the grade of Officer to the following: Dr. James T. Case of Santa Barbara, California and Dr. J. A. del Regato of Colorado Springs, Colorado. This distinguished honor was bestowed on the occasion of the Fifth Inter-American Congress of Radiology which was held in Washington on April 24 to 29, 1955, of which Congress Dr. Case was the President, and Dr. del Regato was the Secretary for Latin America.

The Order of "Carlos J. Finlay" honors the name of the Cuban physician who discovered the transmission of yellow fever by the mosquito. Dr. Fernando Martínez Lamo, senior radiologist of the city of Camaguey, birthplace of Dr. Finlay, was named by the Department of Public Health on behalf of the Cuban government to present the awards and diplomas at the Congress.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The Fortieth Annual Meeting of the Pennsylvania Radiological Society will be held at the Berkshire Hotel, Reading, Pennsylvania, on May 20 and 21, 1955. An interesting program has been arranged. Inquiries concerning the meeting may be addressed to the Secretary, Dr. James M. Converse, 416 Pine St., Williamsport, Pennsylvania.

SYMPOSIUM NEURORADIOLOGICUM

The fourth Symposium Neuroradiologicum will be held in London from September 13 to 17, 1955. Registration will take place on September 12 at the University of London, Malet Street, W.C.1, where the scientific meetings will be held. Radiologists, neurologists and neurosurgeons particularly are welcome.

Subjects for discussion include (1) cerebrovascular disease; (2) the localisation of intracranial tumours by means of isotopes; (3) applications of stereotaxometry; (4) new techniques, and (5) various proferred papers on a variety of neuroradiological subjects. Scientific and technical exhibitions are being arranged.

It is hoped to arrange a joint half-day session with the Second International Congress of Neuropathology which is being held simultaneously in London.

A full social program has been arranged including visits to places of interest for wives and families of members.

Application forms and further information may be obtained from Dr. R. D. Hoare, Secretary, Symposium Neuroradiologicum, The National Hospital for Nervous Diseases, Queen Square, London, W.C.1, England.

TECHNICAL CONFERENCE ON ELECTRICAL TECHNIQUES IN MEDICINE AND BIOLOGY

The Eighth Annual Technical Conference on Electrical Techniques in Medicine and Biology will be held in November, 1955. The Conference is jointly sponsored by the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the Instrument Society of America. Tentative plans call for holding the Conference in Washington, D. C.

The Conference serves as a meeting place for physiologists, biologists, cardiologists, radiologists, physicians, physicists, electronic, electrical, and instrument engineers. A large portion of the registration is drawn from the research groups in universities and industry.

Authors are invited to submit titles of papers for consideration by the Program Committee to E. Dale Trout, Conference Chairman, 4855 Electric Avenue, Milwaukee 1, Wisconsin.

ASOCIACION PUERTORRIQUEÑA DE RADIOLOGIA

At the meeting of the Radiological Society of Puerto Rico held on January 20, 1955, the following new officers were elected for the coming year: *President*, Dr. José Landrón; *Vice-President*, Dr. Guillermo Marquez; *Secretary-Treasurer*, Dr. Rafael A. Blanes, P. O. Box 9067, Santurce, Puerto Rico.

MISSISSIPPI RADIOLOGICAL SOCIETY

At the January, 1955, meeting of the Mississippi Radiological Society the following officers were elected for the coming year: *President*, Dr. John W. Evans, Jackson, Mississippi; *Vice-President*, Dr. Dan Reikes, Hattiesburg, Mississippi; *Secretary*, Dr. James M. Packer, 621 High St., Jackson, Mississippi. Meetings continue to be held at 6 P.M. on the third Thursday in the Edwards Hotel, Jackson, Mississippi.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Skeletal System

Cameron, Bruce M., and Friend, L. F. Osteoid osteoma of the sacrum; report of a case. *J. Bone & Joint Surg.*, July, 1954, *36-A*, 876–877.

The authors report a case of osteoid osteoma of the sacrum because of its unusual location, and also because of the problem it presented in the differential diagnosis of the patient's low back pain. Although it has been stated that osteoid osteoma can occur in any bone, there has not been, to their knowledge, any report of its occurrence in the sacrum.

The patient was a male, aged twenty-one, who had a history of low back pain for one year. On physical examination, the only significant finding was marked point tenderness in the area lying to the immediate right of the fourth sacral process. All laboratory tests including the sedimentation rate were normal. The anteroposterior roentgenogram of the sacrum showed what appeared to be an "extra sacral foramen." It was an osteolytic area, about one-half the size of the normal sacral foramina, in the area of point tenderness. It was surrounded by an area of sclerosis, and in the center there was a small sclerotic nidus. The lateral roentgenogram failed to demonstrate the lesion.

The patient was operated upon. The tumor was a bluish nodule surrounded by sclerotic bone. The microscopic sections showed the typical picture of osteoid osteoma. The patient's operative course was uneventful.—*Ralph S. Bromer, M.D.*

Williams, Robert R., Dahlin, David C., and Ghormley, Ralph K. Giant-cell tumor of bone. *Cancer*, July, 1954, *7*, 764–773.

The authors present a review of the literature on giant cell tumor of bone which reveals how voluminous and confusing the various publications have been over the past years.

This particular study is based on 101 cases of true giant cell tumor of bone. In breaking these cases up into age groups, it was found that about 68 per cent of the patients were between twenty and thirty-nine years of age. Another interesting finding was that about 10 per cent of the patients were less than twenty years of age. The lesions were situated in the epiphysis of long bones of the limbs in more than 80 per cent of the cases and about the knee in approximately 60 per cent. The ilium and sacrum were involved in some 14 per cent. In this series, trauma could not be implicated as a stimulus for the formation of giant cell tumor. Average duration of symptoms before diagnosis was one year with the mass usually palpable in most patients.

An excellent discussion of the pathological characteristics is presented, including the microscopic appearance.

It was noted that microscopically the lesions most commonly confused with giant cell tumors were nonosteogenic fibroma and cysts of the bone. Malignant transformation occurred in 8 of the 101 cases after an appreciable interval following the original histopathological diagnosis. From this series it was found that complete removal of giant cell tumors, either by amputation or excision of the tumor bearing portion of the bone in its entirety, assured the best safety from recurrence and metastasis. Irradiation alone was not responsible for a single cure and it was felt that curettage plus irradiation offered no lower rate of recurrence than did curettage alone. All the patients in whom sarcoma developed following therapy had had irradiation either primarily or for a recurrent lesion which followed other treatment.

True giant cell tumor is a distinct neoplasm with well defined histopathological criteria and it is important to distinguish its variants such as nonosteogenic fibroma, bone cysts and aneurysmal bone cysts.

Detailed tables of treatment and follow-up of the 101 cases are included.—*Claude D. Baker, M.D.*

Eibel, Philip. Dislocation of the interphalangeal joint of the big toe with interposition of a sesamoid bone. *J. Bone & Joint Surg.*, July, 1954, *36-A*, 880–882.

Dislocations of the toes are comparatively rare. The majority of these injuries occur in the great toe at the metatarsophalangeal joint. Of the even rarer interphalangeal dislocations, that of the great toe is again the most common. In this article, a case of interphalangeal dislocation of the big toe with interposition or intra-articular inclusion of the interphalangeal sesamoid is reported. The author states that, to his knowledge, this condition has been recorded only once before in the literature.

The patient had symptoms of dislocation following the stubbing of his right big toe while playing football. Roentgenograms showed an osseous body within the joint which interferred with reduction. This was interpreted as an interphalangeal sesamoid—an opinion which was substantiated by identical findings in the contralateral big toe. Reduction by manipulation was not successful and the patient was operated upon and the dislocation was reduced.

Previous authors have pointed out that the sesamoid is intracapsular and not intratendinous, in contradistinction to current anatomical descriptions. Although the author did not expose the flexor hallucis longus, he feels that this tendon would of necessity have been damaged at operation in the process of freeing the sesamoid from its soft tissue attachments. The fact that this did not occur, as shown by the postoperative course, appears to corroborate these previous observations.—*Ralph S. Bromer, M.D.*

Blood and Lymph System

Rosegay, Harold, and Welch, Keasley. Peripheral collateral circulation between cerebral arteries; a demonstration by angiography of the meningeal arterial anastomoses. *J. Neurosurg.*, July, 1954, *11*, 363–377.

The authors present 3 cases of occlusion of cerebral arteries with subsequent demonstration of filling of the occluded arteries distal to the occlusion by angiography. The filling was from anastomoses with peripheral branches of other cerebral arteries. Two of their cases involved the middle cerebral artery or its branches with collaterals from the anterior cerebral filling the occluded vessel. The other was an occlusion of both anterior cerebral arteries with retrograde collateral filling from the middle cerebral. This latter case did not survive but the middle cerebral occlusions did and one had practically no neurological deficit.

They list the principal anastomotic channels as follows: the internal frontal branches of the callosomarginal, the precentral branch, and the precuneal branch (all from the anterior cerebral) and, respectively, the precentral, central, and parietal branches (all from the middle cerebral); between the angular branch of the middle cerebral and the parieto-occipital branch of the posterior cerebral; and between the precuneal or posterior callosal branches of the anterior cerebral and the parieto-occipital branch of the posterior cerebral. In some cases extensive anastomoses are present between the middle meningeal and cerebral arteries. These collaterals account for the occasional minor neurological deficit sometimes found in occlusions.

The authors stress keeping the blood pressure near normal for the patient if a vascular occlusion is to be produced surgically to avoid permanent damage and allow collateral circulation to function.—*Frank M. Windrow, M.D.*

Di Guglielmo, Lucio, and Guttadauro, Mariano. Anatomic variations in the coronary arteries; and arteriographic study in living subjects. *Acta radiol.*, May, 1954, *41*, 393–416.

The literature provides analysis of the origin and distribution of the coronary arteries in numerous individual cases based principally on postmortem examinations. The anomalies of the coronary arteries may have an influence on the pathologic conditions in the vessels of the heart. The variations may be classified as follows: (1) variations in number; (2) variations in origin; (3) variations in the mode of division and distribution.

(1) The variations in number of coronary arteries usually consist of an increase rather than a decrease. The existence of a single coronary artery is rare. A single coronary artery must alone provide the supply to the whole heart and is, therefore, under greater strain and more easily the site of arteriosclerotic lesions. The occlusion of such an artery will inevitably be fatal since collateral circulation cannot be established.

(2) In the majority of instances the coronary arteries take origin from the superior third of the right and left sinus of the Valsalva, respectively. Rarely one or both of the arteries may take origin in the ascending aorta or in the pulmonary artery. As a rule, it is then the left artery which is anomalous. If a coronary artery has origin in the pulmonary artery, it is usually not compatible with life.

(3) Variations in mode of division and distribution are most commonly encountered in the left coronary artery. One coronary artery may be said to be preponderant when it is more developed and supplies areas which are normally fed by another artery. If the latter fact is not established, the diagnosis of preponderance cannot be made. As in the case of the single coronary artery, preponderance of the coronary artery has serious significance in the event that disease occurs in that artery.

By thoracic aortography it is possible to demonstrate the coronary arteries in living subjects and the authors have used this method to study the coronary arteries in 192 patients. The total material on which this analysis of the coronary arteries is based consists of 399 examinations on 292 patients (192 thoracic aortographies and 207 angiocardiographies). Most of the angiocardiographic studies were performed by the selective method, that is, the contrast material being injected into the right ventricle or directly into the pulmonary artery.

In no instance was there evidence of a coronary artery taking origin from the pulmonary artery and in no instance was there evidence of a single coronary artery or of more than two coronary arteries. In accordance with the previous descriptions by other writers, there were no anomalies in division or distribution of the right coronary artery but both increase and decrease in the usual number of branches of the left artery were found.

The conception of the preponderance of one coronary artery may be confirmed in living subjects but several sources of error must be taken into account. It can be substantiated roentgenologically only when it is clearly evident that such an artery gives rise to one or more important ramifications which normally arise from the other coronary artery and in this way supplies a more extensive area than normally.—*Lois Cowan Collins, M.D.*

Felten, H. Kontrastmittelreaktionen bei der Angiographie. (Contrast medium reactions in angiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, May, 1954, *80*, 575–580.

In urography one usually uses 20 cc. of a 45 per

cent solution, so that 9 gm. of contrast material is injected into the blood stream, while in aortography, 30 cc. of a 60 per cent solution is injected, thus placing 18 gm. of the medium into the blood stream. If repeat examination must be done at the same sitting, a correspondingly greater amount of the contrast medium is administered.

In one-third of the cases there was a more or less extensive spotty reddening of the lower extremities occurring during or immediately following the injection. A similar but less intensive reddening was observed very seldom over the rest of the body, especially over the chest, much later after the injection. Occasionally, there was nausea and very rarely vomiting. Circulatory depression with faint pulse to loss of consciousness may occur. Rarely, laryngospasm and stridor resulted immediately after the injection. It is very important that the patient be observed carefully during and shortly after the injection so that appropriate treatment may be given without delay. No fatalities were noted in over 200 cases and most patients had no complaints on the following day as a result of the examination.

The author uses peridural anesthesia before the aortography. Little or no pain is experienced in the extremities by this anesthesia, in contrast to the case when local anesthesia is employed.

The mechanism of the reaction from the contrast material is not clear. It is definitely not a hypersensitivity to iodine, an idea which is still prevalent, but a reaction to the contrast medium complex. A true acquired allergy is extremely rare. Preliminary test dose of the contrast medium is not an accurate indicator of sensitivity of the patient to the medium. For the individual case the severity of the reaction is a function of the concentration of the injected material into the blood stream, in contrast to the true allergic reaction which is independent of the amount of contrast medium in the tissues.

The prevalent concept today that the reaction to intravascular injection of contrast medium is due to histamine effect has brought on the antihistamine drugs for the proper treatment. Routine prophylactic antihistamine medication is not advised since in most patients there is no unfavorable reaction. The standard method employed for prevention of a reaction is as follows: The patient is observed carefully during the injection, particularly that extremity into which the contrast material is injected, the pulse, and the general condition of the patient. During the developing of the films, the cannula is kept open with a constant flow of saline solution. Should a reaction occur, which is usually first manifested by a spotty reddening of the injected extremity, 2 cc. of Neo-Bridal (a German product of an antihistamine) is forced into the cannula. The reddening usually disappears immediately and no other manifestations arise. Should the reddening not regress, or should generalized symptoms appear, the dose may be repeated once or several times. Under such treatment, repeat examination with contrast material has been done with impunity.—*Samuel Richman, M.D.*

Decker, K., and Holzer, E. Gefässverschlüsse im Carotis- und Vertebralisangiogramm. (Vascular occlusions in carotid and vertebral angiograms.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, May, 1954, *80*, 565–575.

The authors use 8 cc. of contrast medium per injection, with a maximum of 25 cc. during the examination. Three to four lateral skull films are exposed within three to five seconds. The inclusion of the tip of the needle on the roentgenograms has been of aid in clarifying certain findings and in the avoidance of false diagnoses, since the evaluation of changes in the region of the cervical portion of the carotid artery is made easier. Angiography of the contralateral artery in the presence of an acute thrombosis of the carotid artery is dangerous.

Spasm of the intracranial portion of the carotid artery can simulate a thrombosis. Repeat examination is necessary after a short interval. In thrombosis of the middle cerebral vessel, an oblique view may demonstrate the area of involvement more clearly. Thrombosis of the anterior cerebral vessel is a rare finding, and a bilateral angiogram with compression of the contralateral artery is essential. Thrombosis of the vertebral-basilar vessels appears to occur rarely.

Over a five year period, 97 patients were diagnosed as having intracranial vascular thrombosis. Of these the diagnosis was proved by autopsy or operation in 21 cases.

Angiography may visualize variations in the vascular distribution, also the early stages of a thrombosed vessel. The location and extent of the blocked vessel is also shown. Thrombosis of the internal carotid artery begins nearly always at its bifurcation in the neck and terminates in the region of origin of the ophthalmic or the posterior communicating artery. The presence of an embolus in a peripheral small vessel is often noted. A slowing down of the circulation in the damaged vascular area is a characteristic property of many angiograms. This explains the basis for the hypovascular changes of the brain, which do not lead to necrosis. In many cases with fresh apoplectic insults, there are normal angiograms.

Thirty-five cases of thrombosis of the cervical portion of the internal carotid artery were observed. The changes begin at the bifurcation or in the first few centimeters of the internal carotid. The branches of the external carotid are frequently also involved. In 9 instances, the occlusion extended up to the ophthalmic artery. The external collaterals are usually formed by the facial and superficial temporal arteries. It is not clear when in the course of thrombosis of the cervical portion of the carotid artery, clinical

manifestations arise. Seven cases of thrombosis of the intracranial portion of the carotid were noted. A characteristic of the collateral circulation is that the arteries distal to a thrombosed vascular area, filled retrograde, are visualized well on the films on the venous phase. A comparison of the films in the arterial and venous phase can permit one to know the entire extent of the thrombosed area. Re-canalization of small arteries must be ruled out in cases of so-called negative angiograms. The old belief in end arteries of the cerebral blood vessels needs revision. Many anastomotic vessels in the normal brain as well as in those with an infarct show the contary to be the case. Many meningeal artery collaterals can be demonstrated.—*Samuel Richman, M.D.*

Russo, P. E., Parker, J. M., and Mathews, H. H. Changes of the axillary vein after radical mastectomy. *South. M. J.*, May, 1954, *47*, 430–436.

This is a preliminary report of a study to demonstrate occlusion of the axillary vein as a possible cause of lymphedema of the arm following radical mastectomy. The authors have noted, venographically, that the axillary vein may become obstructed as a result of its manipulation during the operation. It may then recanalize after some months. Their series is not yet large enough, or well enough controlled, to prove that this thrombosis is the underlying cause of chronic lymphedema following breast surgery.

Although they note the benefit to be derived from application of an elastic bandage to the arm for two months postoperatively, they cannot yet correlate the clinical result of this prophylactic therapy with the state of the axillary vein as shown by venograms. Further reports are promised.—*Stanley M. Rogoff, M.D.*

Melick, William F. The value of aortography. *South. M. J.*, May, 1954, *47*, 421–426.

The author stresses the value of renal arteriography in the study of patients in whom one kidney may not function well enough to show on the intravenous pyelogram. When a blocked ureter makes it impossible to do retrograde studies, aortography is employed to demonstrate the renal blood supply, from which the surgeon may infer whether the blocked kidney is worth saving at all. The status of the opposite kidney is demonstrated at the same time, helping to establish prognosis if nephrectomy is contemplated. ("A kidney is no better than its blood supply.")

Incidental to this thesis is a discussion of the author's current method of translumbar aortography for visualization of the kidneys. He is now injecting approximately 25 cc. of 70 per cent urokon through a special thin-walled Becton-Dickinson needle which he identifies as Stock Number LNR-T466. This has the advantage of a larger bore relative to its outside diameter, when compared with the conventional stainless steel needles. As connecting tubing, he employs individual, disposable Abbott Venotubes. Although these do not have Luer connectors, they fit well to syringe and needle by simple friction.—*Stanley M. Rogoff, M.D.*

Dalali, Salim J., Plentl, Albert A., and Bachman, Arnold L. The application of pelvic venography to diagnostic problems associated with cancer of the female genital tract. *Surg., Gynec. & Obst.*, June, 1954, *98*, 735–742.

Pelvic venography is discussed as a means of differentiating between lymphatic and venous obstruction as a cause of lower extremity edema. The authors also employ it to localize the node-bearing area at the junction of the internal and external iliac veins, before radiation therapy for carcinoma of the cervix.

An 18 gauge needle is inserted percutaneously into the femoral vein just below the inguinal ligament. A cutdown is necessary when the extremity is very edematous or the femoral vein is thrombosed. Both sides have been examined simultaneously in some of the authors' series of cases.

After a slow saline infusion has been started through a plastic tubing attached to the needle, injection of opaque substance is made by puncturing into the occluded tubing. Between 20 and 50 cc. of neo-iopax, 50 or 70 per cent, are infused into each side at a rate of approximately 2 cc. per second. One important aspect of this procedure is compression of the inferior vena cava for a few minutes before, and also during, injection. This is accomplished by means of an inflated rubber bag applied to the umbilical region.

A single 14 by 17 inch film of the pelvis is exposed about ten seconds after the start of injection. Serial roentgenograms were made in a few of the authors' 40 patients.—*Stanley M. Rogoff, M.D.*

Begg, A. C. Intraosseous venography of the lower limb and pelvis. *Brit. J. Radiol.*, June, 1954, *27*, 318–324.

The author reviews the history of venography dating back to 1938 when dos Santos first investigated acute thrombophlebitis of the leg by injection of contrast medium into the long saphenous vein. Since then various techniques have been devised including the technique used by the author, namely, that of intraosseous injection for ascending venography. This technique is described in detail.

The author lists the various sites of intraosseous injections depending upon the portion of the venous system that is desired to be visualized. Using this particular method of injection the contrast medium passes with rapidity from the bone marrow through

the cortex and periosteum to the deep and superficial veins. These numerous periosteal channels so flood the venous system that a better concentration is obtained in the larger veins than that which follows even a rapid intravenous injection.

The author discusses the attributes of intraosseous venography in relation to deep thrombophlebitis, gravitation ulceration and skin diseases. It is felt that this method has a definite advantage over intravenous injection in deep thrombophlebitis as it is safer, since the medium is not injected directly into the venous system and it is quickly and easily carried away, no matter how poor the superficial veins or how edematous the part. In gravitational ulceration intraosseous venography has been found to give an accurate picture of the condition and function of the deep veins and to demonstrate communicating veins between the deep vessels and between the deep and superficial systems without the necessity of using various artificial measures of tourniquet and compression bandages to deflect the medium from the superficial to the deep veins. This method also enables the clinician to delineate accurately the venous component of any leg dermatosis.

The author concludes by stating that intraosseous venography appears to provide a safe, simple, flexible and certain way of demonstrating the deep venous system of the leg and pelvis. It allows the demonstration of the communicating veins between the superficial and deep systems and shows the retrograde flow which occurs when they become incompetent. It gives an excellent demonstration of the anastomotic circulation resulting from venous thrombosis. Injection of the medium is easy no matter how edematous the leg may be or how poor the superficial venous system. Examination may be completed in five minutes. In 30 patients that have been investigated in the past four months by the author, no untoward incidents have occurred.—*Claude D. Baker, M.D.*

Aurig, G., Süsse, H. J., Kothe, W., and Scholz, O. Zur Kontrastdarstellung des Pfortaderkreislaufes nach perkutaner transperitonealer Milzpunktion. (Contrast studies of the portal venous circulation by percutaneous, transperitoneal splenic puncture.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1954, *81*, 1–8.

This technique is relatively simple and safe and the method is useful to the surgeon. It differentiates between intra- and extrahepatic portal obstruction and clarifies confusing situations in the upper abdomen. In some cases it will spare the patient unnecessary laparotomies. By demonstrating stasis and various collateral channels it helps planning of effective anastomotic procedures. Postoperatively, the function of anastomotic channels can be tested.

Under general anesthesia, a cannula 15 cm. long and with a diameter of 1.2 to 1.5 mm. is introduced into the 9th or 10th intercostal space in the anterior axillary line and the spleen is punctured; 20 to 30 cc. of 70 per cent ioduron is slowly injected and four to five exposures made in rapid succession toward the end of the injection. In the presence of abnormal blood clotting, a finer cannula is used and the test made immediately prior to surgery.

Four cases are discussed in detail and roentgenograms reproduced.—*Frederick M. Reis, M.D.*

Hallenbeck, George A., and Bruwer, André. Portal venography. *Proc. Staff Meet., Mayo Clin.*, June 16, 1954, *29*, 333–341.

The development of operations to accomplish portacaval shunting for decompression of the portal venous bed in portal hypertension with bleeding from esophageal or gastric varices has resulted in a need for accurate preoperative information concerning the status of the portal and splenic veins. Two types of portacaval anastomosis have been found satisfactory for the decrease of portal pressure. In one, the direct portacaval shunt, the portal vein itself is anastomosed to the vena cava; in the other, the end-to-side splenorenal shunt, the end of the splenic vein is sewed to the side of the left renal vein after the spleen has been removed.

Visualization of parts of the portal system by roentgenographic techniques is a fairly recent development; some authors were interested in the extrahepatic and some in the intrahepatic branches of this system.

Two different methods are employed: the splenic portagram, in which the opaque medium is injected percutaneously into the spleen and the portal portagram, in which the opaque medium is injected into a vein in the jejunal mesentery during a laparotomy. Urokon sodium 70 per cent is used. The techniques of the two methods are given in good detail. Several reproductions of splenic portagrams and portal portagrams are shown.

The authors are obtaining splenic portagrams on all patients whose spleens are present and for whom portacaval shunts are planned. Portal portagrams are obtained in patients whose spleens have been previously removed. They dispense with the portal portagrams if a satisfactory splenic portagram is at hand.—*C. Peter Truog, M.D.*

Servello, M., and Dalla Palma, L. La phlébographie hépatique; (aspects normaux). (Hepatic phlebography; normal aspects.) *Presse méd.*, May 26, 1954, *62*, 814–817.

The technique involves rapid injection of 10–20 cc. of organic iodine compound (70 per cent) through a large (9–11) Cournand catheter, introduced via elbow vein and both cavae. Only one film is exposed for each of three areas studied, several maneuvers being recommended to facilitate the penetration into

the respective venous tributary: (a) superior aspect of the right hepatic lobe, corresponding to the second branch of the right hepatic venous trunk, (b) inferior aspect of the right lobe, draining through the lower ramifications of the right hepatic vein, and (c) surface of the left lobe, through the left hepatic vein.

Twelve cases with "normal hepatic function" were studied. In 1 case the procedure could not be completed, because the catheter would not enter the inferior vena cava from the auricular appendage. Contrast material injected under pressure into a small branch will cause intrahepatic extravasation, surprisingly innocuous but resulting in "false" pathological aspects.

The method is considered potentially useful in the diagnosis of vascular thrombosis and dilatation, mainly as an adjunct to splenoportography, perhaps including pressure measurements in the hepatic veins.—*E. R. N. Grigg, M.D.*

RADIATION THERAPY

Malamud, N., Boldrey, E. B., Welch, W. K., and Fadell, E. J. Necrosis of brain and spinal cord following x-ray therapy. *J. Neurosurg.*, July, 1954, *11*, 353–362.

The authors present 2 cases in which the patients displayed a rather rapid central nervous system degeneration several months following roentgen therapy for tumors. The first case was that of a twenty-two year old Air Force man who was treated for a nasopharyngeal carcinoma. He received 3,300 r (in air) to a right lateral port, 1,650 r to a left lateral port and 1,650 r to a posterior port. This was calculated to deliver 5,000 r to the tumor. About a year later he died after a short retrogressive course thought to be degenerative disease of the cervical cord. Autopsy showed an acute necrotizing myelitis associated with fibrinoid degeneration of blood vessels and only a mild glial response.

The other case represented a death twenty-one months following roentgen therapy of a frontal sarcoma. The patient received 2,750 r (measured in air) to each of two lateral ports, 10 by 10 cm, in size, in twenty-five days. The calculated dose at the center of the brain was 3,573 r. This patient showed cystic degeneration and gliosis of the gray matter, demyelinization and gliosis of white matter and hyalinization of the vessels. In the first case the dose was high and it was given rather rapidly (twenty days). In the second case the dose appears to be within safe limits. No explanation is offered.—*Frank M. Windrow, M.D.*

Chao, Jen-Hung, Phillips, Ralph, and Nickson, James J. Roentgen-ray therapy of cerebral metastases. *Cancer*, July, 1954, *7*, 682–689.

This article brings forth many points which are frequently forgotten or not emphasized. Prior to more recent surveys it was felt that the incidence of brain metastases was less than 1 per cent while other surveys reported incidences of as high as 33 per cent. These conclusions have been altered somewhat by the study of the authors who found that the incidence of brain metastases from all types of malignant lesions is approximately 5 per cent. Thus, on the basis of the average yearly incidence of carcinoma deaths it was considered that between 2,000 and 10,000 patients in the United States each year have metastases to the brain.

The various sites of the primary lesion which produces brain metastases are discussed and outlined in table form. The commonest site is the lung. In the past, patients with primary carcinoma elsewhere who later presented cerebral or neurological symptoms have been considered hopeless. Radical neurosurgical procedures have been performed only if a single metastasis was found. The authors use roentgen therapy for the treatment of cerebral metastases exclusively. The technique of irradiation varies with each case. The usual type of roentgen ray used is in the 180 to 250 kv. range but occasionally 1,000 kv. roentgen rays are used. In most cases the authors employ the lower range kilovoltage first and, if an early response is not obtained, the method is changed to supervoltage therapy. Two large contralateral fields are used so that the entire brain is included. The practice of fractionation and protraction of the irradiation is adhered to with the result of fewer cases of reaction. Present indications suggest that the dosage required is a tumor dose of 3,000 to 4,000 r given over a period of three to five weeks.

Thirty-eight cases which were treated by the authors are discussed. Palliation of symptoms followed roentgen therapy in 24 cases. In 12 of the 24 cases the symptoms recurred after a period averaging three and one-half months. One case was still free of symptoms nine years after the irradiation.—*O. M. Richardson, M.D.*

Baird, J. Mason. The value of irradiation in the treatment of certain corneal conditions. *South. M. J.*, July, 1954, *47*, 621–624.

In general, the effectiveness of irradiation in certain corneal conditions is manifested by the relief of pain, resolution of inflammatory processes, epithelization of ulcerated surfaces, and obliteration of neovascularization. Specifically, the corneal lesions that have responded to irradiation are: rosacea keratitis, marginal ulcerative keratitis, epithelial erosions, superficial punctate keratitis, simple corneal ulcers, infected corneal ulcers, corneal abrasions, dendritic keratitis for relief of pain, and Mooren's ulcer.

The dosage and techniques of therapy, using 120 kv. (peak), are presented in detail and the original article is recommended.—*John F. Weigen, M.D.*

Garland, L. H., Hill, H. A., Mottram, M. E., and Sisson, M. A. Cancer of the breast;

the results of radical mastectomy and radiotherapy in two hospitals. *Surg., Gynec. & Obst.*, June, 1954, *98*, 700–704.

The results are reported in two separate series of 100 unselected, consecutive cases of cancer of the female breast, one series from the San Francisco Hospital (S.F.H.), a county institution of 1,200 beds, the other from St. Joseph's Hospital (S.J.H.), an institution operated by the Franciscan Sisters and admitting chiefly private patients. The S.F.H. series included: 22 Stage I cases, 27 Stage II cases, 51 Stage III and IV cases; the S.J.H. series included 37 Stage I cases, 60 Stage II cases and 3 Stage III and IV cases.

The relative five year survival rates were 70 (S.F.H.) and 65 (S.J.H.) per cent respectively for Stage I cases; 40 and 42 per cent respectively for Stage II cases. Considering all patients given some form of treatment to the primary lesion, the survival rates were 37 and 50 per cent respectively, the difference being due to the relatively large number of Stage III and IV cases in the S.F.H. series. The absolute five year survival rate was 25 per cent for the S.F.H. series and 49 per cent for the S.J.H. series.

The results are somewhat inferior to those obtained by McWhirter using a combination of simple mastectomy and vigorous postoperative radiation therapy as the major form of treatment. Considering that McWhirter's figures are on an absolute basis (all patients seen whether accepted for treatment or not) as against the present figures which are largely relative, the fact that McWhirter's results are better tends to speak in favor of the McWhirter technique. —*Chauncey N. Borman, M.D.*

Binks, C., and Sherriff, Edna V. The measurement of skin dose with particular reference to post-operative treatment of carcinoma of breast. *Brit. J. Radiol.*, May, 1954, *27*, 283–288.

The authors describe their method of measuring the skin dose in an oblique irradiation technique such as is used in postoperative irradiation of the breast. They employed several types of phantoms for their experimental survey and extended the study to a series of 50 patients receiving treatment. Wide variations were found between the different methods of measurement which have been advocated in the past.

Measured doses were found to average 15 per cent below those predicted from previous reports on the subject. Approximately 30 per cent variation between maximum and minimum surface doses at various portions of the fields was noted, and the authors raise the question whether the "mean skin dose" as an entity has any real meaning or value. The shape and contour of the chest wall were found to be of far greater importance in determining the skin dose than was the size of the patient. In one case a large area of skin graft, lying a few millimeters below the general level of the chest wall, was shown to be receiving much less than the estimated dose.

In concluding, the authors stress the extreme difficulty of measuring the skin dose in an oblique irradiation technique with any degree of accuracy. Therefore, the measuring techniques should be carefully specified in any published work dealing with radiation therapy.—*Arch H. Hall, M.D.*

Kornelsen, R. O. Tumour dose in the chest cavity. *Brit. J. Radiol.*, May, 1954, *27*, 289–293.

In this article a clinically practical method is given for estimating the tumor dose in the chest from a measurement of the exit dose. The method utilizes the expression $Dx = e^{-u_1(x-a)}$ where x = depth in cm.; Dx = percentage depth dose at x cm.; u^1 = the effective absorption coefficient; and a = the x-intercept at 100 per cent. The measured exit dose is substituted for Dx, and by simple mathematical calculations the per cent tumor dose is easily derived.

A specially constructed ionization chamber was necessary to obtain consistent exit dose readings. The chamber was made as shallow as practical, and a diameter of 3 cm. was chosen to counteract the effect of rib interposition. A body section phantom was built to approximate the human thorax, and Victoreen thimble chamber readings were made at the position of the esophagus. The author experimentally found very good agreement between measured and calculated values—a fact which he believes justifies the use of the method in clinical practice with similar multiportal treatment schemes. Two examples of calculations in actual clinical cases are presented.

The method, of course, enables an estimation of only the central tumor dose. With large fields the variation in dosage at other points may be considerable. Thus this method is most useful in centrally placed lesions where narrow fields are used such as in esophageal tumors.—*Arch H. Hall, M.D.*

Nolan, James F., and DuSault, Lucille. Optimum dosage studies for radiation therapy of carcinoma of the uterine cervix. *Radiology*, June, 1954, *62*, 862–867.

The records of 420 patients treated previously at the Los Angeles Tumor Institute between the years 1933 and 1950 were studied in an attempt to define an optimal dose or range of dosage for carcinoma of the uterine cervix.

The concept of the "supralethal effect" where a regrowth of the tumor in an injured tumor bed as one result of excessive dosage is discussed as one of the causes of treatment failures.

Several graphs are given by the authors, taking into consideration dosage at point A and at point B in their successes and failures along with treatment time. Their conclusion from their data is that proba-

bly 6,000 r plus or minus 1,000 r delivered in an eight-week period is a good optimum range of dosage. It is felt that when dosages are in this general range there will be a higher percentage of clinical successes.—*Donald N. Dysart, M.D.*

Quick, Douglas. The influence of radium on cancer therapy. *Canad. M.A.J.*, Aug., 1954, *71*, 103–109.

A review of the historic achievements of gamma radiation therapy over the years is presented. Attempts at equalling gamma radiation quality through electrical production of roentgen radiation have recently been successful at or above the 2 million volt level. The development of cobalt 60 as a gamma emitter and refinement of the "rotation" technique have both enhanced the efficiency and quality of therapeutic measures available to the radiotherapist.

A third high quality gamma source is the radium element itself. The author describes his own 50 gram converging beam radium unit and cites its efficacy in treating deep-seated and poorly responding lesions. However, he does not believe the high-powered gamma emitters will ever entirely replace intracavitary and interstitial irradiation which have been tried and proved through the years.

There is presented a brief discussion of the more recent unsatisfactorily handled cancer problems including those of lung, esophagus, breast, bladder and prostate, intraoral and advanced female pelvic malignancy. A plea for a more conservative surgical attitude in most of these fields is made, with reservation of the "radical" efforts for the occasional seemingly early case favorable both clinically and technically. External gamma-ray therapy undoubtedly offers more than any former quality of radiation in the direction of increased curability, and increased long and short term palliation.—*Arch H. Hall, M.D.*

Nice, Charles M., and Stenstrom, K. Wilhelm. Irradiation therapy in Hodgkin's disease. *Radiology*, May, 1954, *62*, 641–653.

A review of the entity Hodgkin's disease is presented. Former approaches to therapy along with the more recent concepts regarding classification, and types, methods and results of therapy are discussed.

A series of 208 patients with proved Hodgkin's disease studied and treated at the University of Minnesota Hospitals and followed for five years or longer is evaluated by the authors. Of this group 52 survived five years, giving a survival rate of 25 per cent, and for 167 patients followed ten years or longer, the ten year survival rate is 11 per cent.

The most accurate aid in prognosis is the clinical classification:

Stage I. Involvement of only one lymph node region or a single lesion elsewhere, with no constitutional symptoms.

Stage II. Involvement of two or more proximal lymph node regions confined to either upper or lower trunk, with or without constitutional symptoms.

Stage III. Involvement of multiple lymph node regions with or without constitutional symptoms, or acute Hodgkin's disease with no obvious lymphatic involvement.

For their 20 patients in Stage I, the five year survival rate is 85 per cent, and for 13 of these followed ten years or longer, the ten year survival rate is 77 per cent. In Stage II, there is a 90 per cent survival for 20 patients followed five years, and a 35 per cent survival for 17 patients followed ten years. In the large group of 168 patients with disseminated disease placed in Stage III, the five and ten year survival rates are 10 and 2 per cent respectively.

Treatment of choice in Stage I is either intensive irradiation or, possibly, surgical excision followed immediately by intensive irradiation. An attempt is made to deliver a minimum of 2,000 r tumor dose to the involved chains of lymph nodes in fourteen days, and no prophylactic irradiation is given to other lymph node areas. In Stage II, intensive irradiation to the involved lymph node areas is the procedure of choice. In Stage III, palliative irradiation to reduce tumor masses or relieve symptoms is given. Total body irradiation is occasionally given in small doses to these patients. Nitrogen mustard and TEM are also valuable adjuncts.—*Donald N. Dysart, M.D.*

Heacock, C. H., and Cara, D. J., Jr. Radiation therapy of pancreatitis. *Radiology*, May, 1954, *62*, 654–659.

The authors discuss briefly the etiology, symptoms and diagnosis of pancreatitis which is classified into three categories: "acute pancreatic necrosis," "acute edematous pancreatitis," and "chronic recurrent interstitial pancreatitis."

Fifty-three patients have been treated by roentgen irradiation since 1946. Symptomatic supportive measures were also used in all cases.

All forms of pancreatitis were treated with the following technic and dosage: deep therapy using roentgen rays of 2 mm. Cu half-value layer, generated at 200 kv. was given through 15 by 15 cm. ports at a target-skin distance of 50 cm. Two hundred roentgens, measured in air, were delivered daily for three days, the total dosage being 600 r. Some patients received two or three series of treatments.

The results in these 53 cases were regarded as good in 33, fair in 15 and poor in 5. The authors believe that roentgen therapy, when used early, will prevent abscess formation, necrosis, fibrosis, and possibly recurrences of the disease. Operative procedures might also be rendered unnecessary by this method of treatment.—*Donald N. Dysart, M.D.*

Cosbie, W. G., Anderson, W., Millar, O. B., and Bunker, M. L. Carcinoma of the body of the uterus. *Am. J. Obst. & Cynec.*, May, 1954, *67*, 1014–1027.

The authors present their observations of 421 patients with endometrial cancer seen in the gynecological clinics of the Toronto General Hospital and Ontario Institute of Radiotherapy from 1937 to 1952.

Intracavitary radium followed in about six weeks by total hysterectomy and bilateral salpingo-oöphorectomy was the routine planned treatment in operable cases. Lymph nodes were not removed as a rule. Those patients who were not operated upon because they were poor surgical risks or who were beyond hope of a surgical cure were treated by intravaginal as well as intracavitary radium and high voltage therapy at 400 kv. delivered on six pelvic ports. A cancer-lethal dose of radiation could be given to the tumor much more rapidly and efficiently with radium than high voltage therapy according to the authors' discussion.

Two or three tandem pairs with a length of 4.5 cm. and 6 cm. respectively and containing a total of 60 mg. of radium were used in smaller uteri. Employing the principle advocated by Heyman, multiple applicators were used in the large uterine cavity and the uterine cavity distorted by fibroids. The pattern of isodose curves plotted about such applicators indicated less surface intensity was delivered by multiple applicators than with either of the single applicators but the depth doses were equivalent. The shorter applicator caused the most severe intensity.

Preoperative radiation therapy was found to cause an appreciable decrease in the size of the enlarged uterus and cessation of bleeding and discharge.

The trend in recent years has been toward a decrease in the number of patients who were only "technically operable" and who are now better surgical risks with better medical supervision and improved anesthesia. The dosage of uterine radium has been standardized. Increased application of the planned method outlined is believed to have also contributed to the improvement of the three year survival of all patients seen at the Toronto General Hospital from 56.4 per cent in the 1937–1947 period to 70.9 per cent in the 1948–1949 period.

The authors pointed out that the effect of therapeutic radiation may render the positive identification of residual tumor extremely difficult. Painstaking evaluation of the pathological specimen becomes a matter of great importance if the presence of residual tumor is to be used as an indication for further therapy.—*Thomas B. Efford, M.D.*

Rübe, W. Hypoplasia mammae unilateralis durch Radiumbestrahlung eines Haemangioms. (Unilateral mammary hypoplasia from radium treatment of a hemangioma.) *Strahlentherapie*, 1954, *94*, 561–565.

A fourteen year old girl with an aplastic right mammary gland had a history of having a hemangioma of the right areola treated with radium at the age of three months. The hemangioma had disappeared. The tissue dose to the areolar area is estimated at 3×400 r administered within four weeks (the treatment record was no longer available).

Four additional instances of failure of a mammary gland to develop after being irradiated in childhood are cited.

Prepubertal mammary tissue must be considered as radiosensitive, probably because of its undifferentiated condition. Mature mammary tissue is, on the contrary, highly resistant to radiation damage. Radiation tolerance dose must therefore depend on the age of the patient and on the degree of differentiation of the tissue irradiated.— *Henry G. Moehring, M.D.*

O'Brien, Frederick W., and O'Brien, Frederick W., Jr. Surgery and radiation in cancer of the female breast. *Radiology*, Aug., 1954, *63*, 192–200.

The role of surgery as it is utilized in various medical centers for the treatment of cancer of the female breast is discussed. Attention is called to the importance of the internal mammary chain of lymph nodes as a not infrequent site of metastatic spread. Involvement of these lymph nodes, if known, would mean the carcinoma would belong in Stage III instead of Stage II.

The nature of the development of the distressing sequel, lymphedema, is still poorly understood. It is felt that it is more likely due to actual postoperative changes than to postirradiation fibrosis.

The place of irradiation in the treatment of cancer of the breast is considered at length. The authors do not believe that radiation in sufficient amount to sterilize the tumor is either desirable or necessary except in inoperable cases, or where there has been an incomplete surgical procedure. Complementary preoperative irradiation with the idea of immobilizing and modifying the undifferentiated young neoplastic cells is suggested as advisable. Amounts of radiation given within a reasonable time and without the production of fibrosis and then followed by surgical intervention before new young neoplastic cells appear would seem to offer a means of improving the cure rate.

Medical centers in Europe report better five year survival rates with preoperative irradiation than when no prior irradiation is given.

The authors' experience has been confined to postoperative roentgen irradiation. Their series of 152 unselected cases of cancer of the breast is reviewed. Total skin doses of 2,500 to 3,000 r with 400 kv. and a special Thoraeus filter (Half-value layer of

5 mm. Cu) at 50 cm. target-skin distance are given to the axilla and supraclavicular areas using multiple ports.

When treating scar recurrences, 200 kv. with a half-value layer of 0.9 mm. Cu is used and a total air dose of about 2,000 r is given. Relief of bone pain is obtained with 800 to 1,000 r.

Of the 152 patients, 58 (38 per cent) are living and well without demonstrable disease at the end of five years.

Mention is made of the scanning technique where 2 mev. radiation is used to deliver a substantially uniform dose over a region extending from the axilla to the mediastinum. Utilizing two methods of rotation an attempt is made to deliver a depth dose of 6,000 r to the tissues bounded by the pleura on the inside and the subcutaneous tissues on the outside, with only two treatment fields. Freedom from pulmonary fibrosis is a striking feature of this technique.

In conclusion, the authors state that surgical-radiotherapy consultation before, during, and after the first planned treatment would offer to the patient the best chance available.—*Donald N. Dysart, M.D.*

Wood, Ernest H., Berne, Alfred S., and Taveras, Juan M. The value of radiation therapy in the management of intrinsic tumors of the spinal cord. *Radiology*, July, 1954, *63*, 11–24.

Spinal cord glial tumors comprise about 7 per cent of the central nervous system glial tumors. Sixty-two verified cases were analyzed by the authors. Of this group 39 were classified pathologically, and in 23 the diagnosis was established only by surgical gross inspection. Approximately two-thirds of the histopathologically classified tumors were ependymoma and approximately one-third were astrocytoma, while 4 patients had miscellaneous tumors, two of which were lipoma.

The average age of the entire group of patients when first seen was thirty-seven years. The tumors seemed to occur at an earlier age in men than in women. A caudal location was more common in this series, while other writers have found the tumors more common above the conus.

The authors have found that the average longevity is greater when immediate postoperative radiation therapy is administered than with surgery alone, regardless of the type of glioma present. Recovery of function following surgical treatment is enhanced when radiation therapy is utilized. Advancement of disability if recurrence takes place is usually inhibited by radiation therapy. Pain is almost always alleviated. The present trend is to conservative surgery, consisting of decompression, evacuation of areas of cystic degeneration and removal of accessible portions of tumor. The trend also exists toward more intensive radiation therapy.

The radiation therapy was administered with roentgen rays generated at approximately 200 kv. with 1 mm. Cu and 1 mm. Al added filtration. Half-value layer varied from 0.95 to 1.2 mm. Cu. A target-skin distance of 50 cm. was used; 200 r (in air) were delivered at each treatment which was given daily for varying periods. Usually a single appropriate sized posterior port was employed although occasionally anterior, lateral and oblique fields were also used. An attempt was made to deliver a tumor dose of 1,500 to 2,000 r in ten to twenty days, or longer if necessary, with the series being repeated several times, usually coincident with exacerbation of symptoms.

The result of this type of treatment is gratifying. In some patients permanent control of the neoplastic process is accomplished and in the others palliation gives many months and often years of comfortable and useful existence.—*D. N. Dysart, M.D.*

Lutterbeck, Eugene F., Hummon, Irvin F., Wolcott, Rolla R., and Johansen, Frederick A. The effect of roentgen rays on lepromatous leprosy. *Radiology*, July, 1954, *63*, 1–10.

In a review of the literature the authors found that radium and roentgen therapy was used in the treatment of lepromatous lesions as early as 1901. Although dosage factors were not precisely recorded, it is concluded that, in general, poor results were reported by those using small doses and good results by those using larger doses.

The authors present 6 case reports in which a Philips contact therapy machine was used. The unit operates at 50 kv., 2 ma., with 18 mm. anode-skin distance. The output is 10,000 r per minute. The half-value layer is 0.3 mm. aluminum. In the 6 patients with lepromatous leprosy, 23 different areas were treated with single doses of contact irradiation ranging from 1,000 to 6,000 r.

The following conclusions were made:

1. Ionizing radiation is effective in causing flattening and atrophy of lepromatous skin lesions.
2. At least 2,000 r are required to cause such changes.
3. Ionizing rays do not cause any uniform change in bacillary findings.
4. Contact roentgen irradiation affects only superficial structures of the skin. In the doses used it does not cause atrophy or regression of lepromatous lesions in the dermis or subcutaneous tissues.
5. No local recurrences were observed in irradiated areas during a two year observation period.
6. Irradiated areas can be invaded by growing adjacent lepromatous lesions.
7. Local radiation effects on skin lesions do not change the general course of leprosy.—*E. E. Seedorf, M.D.*

Baud, Juliette. Quelques réflexions à propos d'une statistique générale portant sur 3.327

cas d'épithélioma du col de l'utérus traités par les radiations de 1919 à 1947 à la Fondation Curie. (Some reflections with regard to general statistics on 3,327 cases of epithelioma of the uterine cervix treated by radiations from 1919 to 1947 at Fondation Curie.) *Gynéc. et obst.*, 1954, *53*, 408–416.

This study is based on the following material: (a) From 1919 to 1928, 398 patients (64 Stage I, 182 Stage II, 122 Stage III, 30 Stage IV) received intracavitary radium therapy only. Peripelvic roentgen therapy was added in 148, teleradium therapy in 161; 62 were irradiated only transcutaneously. (b) From 1929 to 1941, 1,188 had combined internal and external treatment, 187 (105 Stage I, 61 Stage II, 11 Stage III, 10 Stage IV) internal alone, 55 external alone. (c) From 1942 to 1947, 11 (7 Stage I, 3 Stage II, 1 Stage III) were treated exclusively by radium application, 117 exclusively by peripelvic irradiation (46 with 180 kv.p., 59 with 500 kv.p., 12 with radium bomb), and 1,000 had both (295 with 180 kv.p., 584 with 500 kv.p., 121 with teleradium therapy). No mention is made of intravaginal cones.

The "results" (probably five year cures) of combined internal and external irradiation are summarized in the following table:

	1919–1928		1929–1941		1942–1947	
Stage I	40/70	57%	148/228	64%	180/235	77%
Stage II	106/290	36%	297/652	45%	295/654	45%
Stage III	70/318	22%	134/421	31%	33/219	15%
Stage IV	1/91	1%	19/129	14%	0/20	0%
Total	217/769	28%	598/1430	41%	598/1128	45%

Statistical inconsistencies (worsening of Stages III and IV results) are due to adoption of the League of Nations classification in 1939. Success or failure did not seem to be related to the anatomoclinical form. Chances of survival were the same even for 124 cases of carcinoma of the cervical stump and 44 developed during pregnancy.

The radium applicator used is a rubber tube, covered with aluminum foil (6 mm. external diameter). The colpostats, made of cork, are spaced by springs. The dosage is 24 to 36 (rarely 40) millicuries destroyed (3,200, 4,700, and 5,350 mg./hr.) in the canal, 24 to 36 mc. destroyed in the vagina. Packing with gauze maintains the colpostats in place, and protects the cul-de-sacs. Among the 105 Stage I cases treated from 1929 to 1941 by radium application alone, 74 (70 per cent) were alive and free of cancer at 5–24 years after treatment, 13 had succumbed to intercurrent diseases, while in 18 there were recurrences (locally in 3, in the pelvis in 6, locally and in the pelvis in 7, metastatic in 2). From 1929 to 1941, 61 Stage II cases received intracavitary radium therapy only, and 27 (44 per cent) were apparently cured 5–18 years after completion, 10 had died of other causes, and 24 had recurrences (3 locally, 6 in the pelvis, 12 both locally and in the pelvis, 3 metastatic).

By comparison, from 1929 to 1941, 122 Stage I cases were given internal and external irradiation: 77 (63 per cent) seemed cured, 4 could not be traced, 6 had died of unrelated causes, 30 recurred (1 locally, 10 in the pelvis, 17 locally and in the pelvis, 2 with metastases), and in 5 the failure was unidentified. From 1941 to 1947, 147 Stage I patients were treated with radium and external therapy: 112 (76 per cent) appeared cured, 2 were untraceable, 2 had died of intercurrent diseases, 29 exhibited recurrences (1 locally, 8 in the pelvis, 17 both locally and in the pelvis, 3 by metastases), and in 2 the failure was of unknown cause.

Most of the failures in Stage I cases were due to residual (latent) cancer cells, which caused recurrences 3–4 years after completion of therapy. Another group, although correctly treated and showing (superficial) cervical cicatrization, went unabated to the inexorable death within 6 months to one year. In Stage II failures, non-sterilization occurs in one-third of the cases, with survival of less than one year, but late recurrences are also seen: between 1937 and 1947 there were 13 Stage II patients who survived over 5 years, despite evidence of cancer (one of them was still alive after 11 years). In Stage III failures, irradiation usually fails to stop the growth; in recurrences, pelvic pain is a premonitory sign. As a rule, infiltrated parametria are harder to control than extensive vaginal involvement.

In 8–9 per cent of the 5 year cures, recurrences appeared between 5 and 10 years, in 4 per cent later than 10 years, once 20 years after completion of therapy. They were seldom in the vagina or cervix, mostly in the pelvis, often metastatic, and no benefit could be derived from either surgery or irradiation. Pseudorecurrences were also encountered, such as vaginal ulceration (histologically negative) or pelvic induration, both receding spontaneously over a period up to 2–3 years.

Infectious complications are today of little importance. Just as in exophytic tumors, it is sometimes

best to start with external irradiation; the radium can be applied after local clearance. *Rectal complications* are common. In 30 per cent of cases, a transient rectitis appeared shortly after the intracavitary radium therapy, but disappeared without sequels in 10–25 days. In the period 1929–1941, among patients treated with internal and external irradiation, 18 per cent had symptoms of varying degree (from diarrhea and melena to edema of the rectum and occasionally intestinal obstruction) for about one year, 6 per cent for several years, while 4 per cent had definite local sclerosis and/or stenosis. These complications were more often seen from 1942 to 1947, due to larger transcutaneous dosage and longer survival: 3 cases of rectovaginal fistula (neoplasm cured) and 2 of anal stenosis requiring colostomy are mentioned. As a result, they reduced the radium dosage in advanced cases when conspicuous peripelvic irradiation was given. *Cutaneous complications* are usually benign (telangiectasis) or rare (dyschromia). A sarcoma of the abdominal wall appeared 6 years after treatment in a cured patient. *Osseous complications* are exceptional, and always due to external irradiation. From 1942 to 1947 there were 5 fractures of the femoral neck (2, 4, 5, 7, and 9 years after treatment), 4 of them are living after 6–10 years, 1 healed without sequels, 2 with severe shortening, 1 is a nonunion.

The intracavitary radium application is intended as the cancerocidal agent. Unfortunately, the neoplasm usually extends beyond the confines detectable by clinical investigation, and therefore external irradiation must be added, in order to raise the adnexal dose to acceptable levels. Exacting techniques can achieve this aim, and at the same time will avoid, in most cases, rectal and osseous complications.—*E. R. N. Grigg, M.D.*

Fricke, Robert E., Van Herik, Martin, and Soule, Edward H. Treatment of rare lesions of the uterus and vagina. *Radiology*, Sept., 1954, *63*, 353–360.

A patient found to have a primary lymphosarcoma of the cervix prompted the authors to make a study of the rare pelvic cancers treated at the Mayo Clinic. They found that during the decade from 1935 to 1944, 2,178 patients with pelvic cancer were treated. Of these, 27 presented unusual pelvic tumors.

The cervix uteri showed the lowest evidence of unusual malignant growth with only 2 cases among 1,273 patients treated with the more usual types of cancer. Both of these patients had hemangioendotheliomas. One was treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy with no irradiation. This patient was living with no recurrence twelve years after operation. The other received a complete course of radium therapy, employing an intensive broken-dose method, irradiating the entire cervical canal, vaginal cavity, and endometrium with about eight applications of radium over a period of three to four weeks. Supplementary roentgen therapy was also given then and repeated six and nine months later. Pulmonary metastases led to this patient's death about two and one-half years after the initial treatment.

Of 116 patients with primary vaginal cancer, 5 showed unusual lesions. One had a sarcoma botryoides, 2 had melanoepitheliomas, and 2 had leiomyosarcomas. Treatment varied with each case, depending upon the findings. None of the 5 patients did well with either surgical or radiation therapy.

Twenty unusual malignancies were found among 789 cancers of the corpus uteri. One was a chorionepithelioma, 1 was a mixed mesodermal tumor with cross striations, 1 was a carcinosarcoma, and 17 were leiomyosarcomas.

Surgical treatment consisting of total abdominal hysterectomy and bilateral salpingo-oophorectomy was used in 18 patients. Eight patients received surgical treatment plus irradiation. Of these 20 patients, 6 are living and apparently well, eight to thirteen years after treatment. Four of these had surgical treatment only; 2 had surgical treatment plus postoperative roentgen therapy.

In general, irradiation has played a minor therapeutic role, as all of the above tumors are radioresistant with the exception of the hemangioendothelioma of the cervix. Surgical treatment has proved the best means of attack on these tumors. In some patients who are surgical risks, irradiation, however, may at least give worthwhile palliation even in some radioresistant neoplasms.—*Donald N. Dysart, M.D.*

RADIOISOTOPES

Thode, Harry G., Jaimet, Charles H., and Kirkwood, Samuel. Studies and diagnostic tests of salivary-gland and thyroid-gland function with radioiodine. *New England J. Med.*, July 22, 1954, *251*, 129–134.

The uptake of radioactive iodine by the salivary glands may be measured in the saliva with a scintillation counter. It is stated that this augments the 24 hour uptake measurements over the thyroid gland and the conversion ratio studies presently used. Inasmuch as the uptake of radioactive iodine in the salivary glands is related inversely to that of the thyroid, it is expected that this test will be particularly valuable in the diagnosis of hypothyroidism.

A method is described for conducting this examination, and the uptake in the saliva in 24 hours is recorded in counts per minute rather than as a percentage. Eight patients were studied and the thyroid uptake, conversion ratio, saliva uptake, saliva-plasma ratio, and saliva-protein bound iodine (PBI) ratio are compared in each patient. The saliva-PBI comparison is the most reliable, according to the

authors, and offers the greatest degree of correlation. —*George Roberts, M.D.*

Kurland, G. S., Freedberg, A. S., and Fishman, J. Effect of thyrotropin on changes in thyroid function following administration of I^{131} to euthyroid cardiac patients. *J. Clin. Endocrinol. & Metabol.*, May, 1954, *14*, 572–578.

The effect of thyrotropic hormone on thyroid function following large therapeutic doses of radioiodine was studied in 8 patients. A previous study by these authors, demonstrating normal thyroid histology seven days following a therapeutic dose of radioiodine, even though function was depressed, led them to investigate the possibility of reversing the functional change by the use of the thyroid stimulating hormone. Thyroid function in this study is measured by the thyroid uptake of radioiodine, and the time that this iodine is retained by the gland.

For control studies, the effects of large therapeutic doses of radioiodine given to 27 cardiac patients are tabulated. The average uptake of the first therapeutic dose was 33 per cent, of the second dose 11 per cent; average biological half-life of the first dose was 6.0 days, of the second dose was 1.9 days. The lower uptake and shorter retention of the second dose is interpreted as indicating depressed function.

Eight other patients received thyrotropic hormone before the second dose. Four patients received 12.1 U.S.P. units of thyrotropin on the sixth and on the seventh days after the first radioiodine dose; the average uptake values were 33 per cent for the first dose, 44 per cent for the second; and the average biological half-lives were respectively 7.3 days and 6.9 days. Similar results were obtained with 4 other patients to whom thyrotropic hormone was administered from 14 to 54 days after the first therapeutic dose. Thyrotropic hormone had no effect on the radioiodine uptake in a patient in whom myxedema had been induced 18 months previously.—*R. Kenneth Loeffler, M.D.*

Kirkland, Richard H. Impaired organic binding of radioiodine by the thyroid following radioiodine treatment of hyperthyroidism. *J. Clin. Endocrinol. & Metabol.*, May, 1954, *14*, 565–571.

Ten patients, treated for hyperthyroidism with radioiodine, were studied to demonstrate alteration in thyroid function resulting from this treatment. Previous workers had shown that thyroid glands under the influence of thiouracil are capable of accumulating part of a tracer dose of radioiodine, but that such glands are unable to convert the inorganic iodide into the organic form. This impairment of function is manifest in two ways: (1) the iodine uptake curve is distinctive, reaching maximum uptake in two hours, with no significant change in the next three hours, and (2), much of this iodine is rapidly released from the gland as inorganic iodide following the admistration of sodium thiocyanate.

Using these criteria, 27 patients adequately treated with radioiodine had uptake curves determined, usually at eight weeks following therapy. Ten of these showed the "injury curve" with maximum uptake at two hours. Administration of thiocyanate to these 10 resulted in an average loss of 54 per cent of the activity, compared with a loss of only 3 per cent in a group of 20 control patients. These results are interpreted to show an impairment in the organic binding of iodide.

The "injury curve" was observed in 1 patient with hyperthyroidism who received roentgen therapy. Two patients who showed the "injury curve" eight weeks following therapy, even though still clinically toxic at that time, became clinically euthyroid by the following month without further therapy.

It is believed that this impairment of organic binding of accumulated iodide is present in most cases of hyperthyroidism treated with radioiodine, but that it is a transient state which may not be detected unless studies are carried out at the right time.—*R. Kenneth Loeffler, M.D.*

Phillips, A. F. The gamma-ray dose in carcinoma of the thyroid treated by radio-iodine. *Acta radiol.*, June, 1954, *6*, 533–544.

The irregularity of distribution of the radioactive iodine taken up by carcinoma of the thyroid, and the short range of beta rays emitted by I^{131}, are likely to leave certain regions of the tumor virtually unirradiated by these beta rays. Correlation of histological and autoradiographic studies showed carcinoma cells in fibrotic regions where there was no appreciable uptake of radioiodine and which were beyond the effective range of beta rays.

The dosage from radiation due to gamma rays from I^{131}, on the other hand, was found in two surgical specimens to be similar to the dose calculated on the basis of uniform distribution of the isotope. Gamma-ray dosage of a therapeutically useful range, however, would require the administration of radioiodine in amounts that would be impractical.

The author suggests that other radioactive isotopes may eventually prove more useful in treatment of carcinoma of the thyroid, if made available in sufficient quantity. For example, I^{124} emits beta rays which penetrate about four times as far as the beta rays from I^{131}, and also emits more energy as gamma rays per disintegration.—*Thomas B. Efford, M.D.*

Badenoch, John, and Callender, Sheila T. The use of radioactive iron in the investigation of anaemia. *Brit. J. Radiol.*, July, 1954, *27*, 381–386.

Of the 4 to 5 gm. of iron in the normal adult male,

60 to 70 per cent is in the hemoglobin, 15 per cent in the storage iron, 0.1 per cent in transport iron in plasma, 0.1 per cent in respiratory enzymes, and 3 to 5 per cent in myoglobin. Iron is ionized by gastric juices and absorbed in the upper small intestine. Only about 10 per cent of ingested iron is normally absorbed and only a small amount of that absorbed is excreted, it being stored and used again in red blood cell formation. Absorption is increased in iron-deficiency states, as has been previously known, but is confirmed by oral administration of radioactive iron and then measuring radioactivity of blood and stools. In aplastic anemia, uptake of iron by the red blood cells is diminished. Fe^{59} given intravenously is not mixed uniformly with stored iron, suggesting that the most recently administered iron is more readily mobilized. The rate of disappearance of iron from plasma is rapid in hypochromic anemia and polycythemia vera, and slow in aplastic anemia. This provides a check on the value of roentgen and P^{32} therapy of polycythemia vera, as the plasma disappearance rate returns to normal following effective therapy.

The authors studied a group of patients with hypochromic anemia who were refractory to oral iron. Eight out of 18 patients were found by this and other tests to have idiopathic steatorrhea. The amount of iron absorbed in 13 normal patients and in 6 patients with simple hypochromic anemia was greater than in the patients with idiopathic steatorrhea. Intravenous iron in the latter was utilized normally, although oral iron was poorly absorbed.—*George Roberts, M.D.*

BELCHER, E. H., GILBERT, G. F., and LAMERTON, L. F. Experimental studies with radioactive iron. *Brit. J. Radiol.*, July, 1954, *27*, 387–392.

Preparation, administration, and determination of absorption and excretion of radioactive iron in rats are fully described. Of particular interest to the authors is the evaluation of the effects on iron uptake of roentgen radiation administered with 250 kv. (peak) and a half-value layer of 1.5 mm. Cu, 24 and 48 hours previously. A dose of 50 r whole body radiation 48 hours prior to iron administration reduces uptake 50 per cent in one day, with recovery to 80 per cent in 7 days; whereas a dose of 200 r similarly given causes almost complete suppression of uptake with slower recovery. The minimal amount causing detectable depression is 30 r.—*George Roberts, M.D.*

LOCKSLEY, HERBERT B., SWEET, WILLIAM H., POWSNER, HENRY J., and DOW, ELIAS. Suitability of tumor-bearing mice for predicting relative usefulness of isotopes in brain tumors; comparative clinical and laboratory study in localization and treatment of brain tumors with P^{32}, Na^{24}, K^{42}, and sodium borate. *A.M.A. Arch. Neurol. & Psychiat.*, June, 1954, *71*, 684–698.

In connection with different investigations, it was necessary to screen a variety of isotopes. This could best be done under carefully controlled conditions using a uniform tumor in a pure strain animal. Pure strain mice were used. The mouse brain tumor was originally induced by 20 methylcholanthrene and was then passed through over 50 generations by subcutaneous transplantation.

Observations were made on mice by using various isotopes. It was found that pure-strain mice provided coherent comparative data which can be obtained rapidly and consistently.

Comparative studies in mice and patients with P^{32}, K^{42}, and sodium borate have demonstrated close agreement in the concentration ratios observed between tumor and brain. Measurements of the extracellular sodium space for various organs in different animals also showed close agreement. This favorable comparison of data in mice and patients was further substantiated in a series of positron emitting isotopes, including Mn^{52}, Rb^{84}, and As^{74}.

The most rapid and valid method found for obtaining these correlation data in patients is an extension of the Geiger probe technique of tumor localization, whereby continuous uptake curves may be obtained over a period of hours or days.—*Frank J. Rigos, M.D.*

BAKAY, LOUIS. Studies on blood-brain barrier with radioactive phosphorus. IV. Spatial aspects of phosphate exchange between plasma and brain. *A.M.A. Arch. Neurol. & Psychiat.*, June, 1954, *71*, 673–683.

The concentration of P^{32} and the specific activity of plasma, cerebrospinal fluid, and various parts of the brain were determined in cats over a period of from thirty minutes to three weeks after a single intravenous injection of the isotope.

The concentration curves indicate an early exchange of phosphate between the cerebrospinal fluid and the central nervous system. Diffusion of P^{32} from the ventricular fluid into the surrounding brain tissue can be delayed by obliterating the ventricle with paraffin prior to the injection of the isotope.

The distribution of P^{32} in various parts of the brain, shortly after its injection, is the same whether it has been injected intravenously or directly into the cerebrospinal fluid. A much higher dose is required to obtain the same concentration in the central nervous system if the intravenous injection is used.

Higher phosphate exchange was found in the surface areas, both externally and internally, than that found in the depth of the brain. An equilibrium between these different areas was approached but not quite reached.

Plasma phosphate enters the central nervous sys-

tem by transcapillary exchange and by an indirect route, using the cerebrospinal fluid as intermediary. A theory combining these two factors and dependent upon permeability and diffusion is presented.—*Frank J. Rigos, M.D.*

Read, Raymond C., Wilson, Graham W., and Gardner, Frank H. The use of radioactive sodium chromate to evaluate the life span of the red blood cell in health and certain hematologic disorders. *Am. J. M. Sc.*, July, 1954, *228*, 40–52.

Small samples of blood from both normal and anemic individuals have been tagged with radioactive chromium using a technique which avoids damaging the red cells. The blood was withdrawn and incubated with less than 10 micrograms of chromium per cc. of red blood cells containing approximately 100 millicuries of Cr^{51} activity. Usually 30 cc of whole blood was withdrawn and incubated for one-half hour with sodium chromate tracer. After the addition of 50 mg. ascorbic acid the blood was reinjected.

The survival of the tagged cells after reinjection has been followed and compared in some cases with simultaneous Ashby studies.

The results show that in healthy individuals, cells tagged with chromium have a normal life span. The radioactivity leaves the circulation in an exponential fashion which is reproducible in healthy men.

In the various hemolytic and hypoplastic disorders studied, the manner of removal of the tagged cells from the circulation was in essential agreement with the other hematological data and did not appear to be significantly affected by the labelling process itself.

The results are discussed and the advantages and disadvantages of this technique compared with the classical Ashby method.—*Frank J. Rigos, M.D.*

Kirn, F. S., Kennedy, R. J., and Wyckoff, H. O. The attenuation of gamma rays at oblique incidence. *Radiology*, July, 1954, *63*, 94–104.

The authors present data relative to attenuation of radiation incident obliquely upon barriers of lead, concrete or concrete-equivalent material.

Gamma radiation from cobalt 60, cesium 137 and gold 198 was measured at angles of incidence of 0 degrees, 30 degrees, 50 degrees, 60 degrees and 70 degrees. Results show that for oblique angles of incidence, the Compton scattered radiation may have shorter path lengths through the barrier. For larger angles of incidence, the obliquity effect must be considered in designing barrier requirements. It is demonstrated that for a diverging cone of radiation the effect is not too significant for attenuations less than 100, and also that the addition of a layer of lead behind a low atomic number barrier can be effective in reducing the thickness requirements of the barrier if the energies in use are below the 0.7 mev. range.—*A. Ralph Watson, M.D.*

Cooper, John A. D., Bulkley, George J., and O'Conor, Vincent J. Intraprostatic injection of radioactive colloids. I. Distribution and excretion following injection in the dog. *J. Urol.*, May, 1954, *71*, 624–627.

This is a preliminary report of the distribution of colloidal chromic phosphate and colloidal gold in the tissues, plasma and urine of experimental animals following the intraprostatic injection of these materials.

Under anesthesia the prostate gland of the animal was exposed through a midline suprapubic incision. The radioactive colloid in doses of 2 to 4 cc. containing 3 to 9 millicuries was injected. The incision was then closed and the animals were placed in metabolic cages for collection of urine for radioactive assay. Blood samples were obtained at intervals for estimating the amount of radioactive colloid present in the circulation. The dogs injected with chromic phosphate were sacrificed at the end of two weeks and those injected with radiogold were sacrificed at the end of one week.

The amount of colloid in various tissues was determined by utilizing a weighed sample in 5 cc. of water in a glass homogenizer. In the case of the prostate gland the entire organ was homogenized. The radioactivity of the specimen was determined by counting with an end window Geiger tube.

The urinary excretion of radioactive colloidal gold and chromic phosphate varied considerably with the individual dog and with the size of the particles injected. The large excretion during the first twenty-four hour interval was attributed to the entrance of the colloid into the urethra and bladder directly from the prostate at the time of injection or shortly thereafter. No relation could be established between the size of the prostate gland or the amount of solution injected per gram of tissue and the total urinary excretion. The figures for the urinary excretion of colloidal gold varied from 3 to 60 per cent of the injected dose during a period of seven days. Preliminary data on urinary excretion of radiogold from human beings who have received intraprostatic injections indicate that much smaller amounts appear in the urine of these individuals than are found in the dog.

The plasma concentration of the colloids was fairly constant over a seven day period. This probably indicates a continual entrance of the colloids into the circulation from the prostatic source.

The failure of the colloids to remain at the site of injection may be due to diffusion along the fascial planes of the pelvis. Radioactive survey indicated a large amount of radioactivity remained in the pelvis

after the removal of the prostate and urinary bladder. This was attributed to the presence of radioactive material in the fascial planes as well as in the pelvic lymph nodes.

Following the injection of colloidal gold into the prostate it was found that 1.154 per cent, of the total amount injected, remained in the prostate per gram of prostatic tissue. This corresponded to 10.5 per cent in the total organ. 14.2 per cent of the original colloidal gold was retained in the liver seven days after its injection into the prostate. A negligible amount was found in the lung, kidney and bladder. The lymph nodes contained 3.6 per cent per gram of involved tissue.

The histological studies on tissues removed from animals sacrificed at various times following injection are to be published.—*George W. Chamberlin, M.D.*

FLOCKS, R. H., KERR, H. D., ELKINS, H. B., and CULP, D. A. The treatment of carcinoma of the prostate by interstitial radiation with radioactive gold (Au^{198}): a follow-up report. *J. Urol.*, May, 1954, *71*, 628–633.

As a result of experience in 130 patients, the authors have found that the most satisfactory dosage has been 2 millicuries per gram of tissue with an upper limit of 150 millicuries total dose. The purpose of the radioactive gold injection is to obtain a very large dose of beta radiation into the local malignant tissues in the prostate gland with very little irradiation of the bladder and rectum. The total volume of solution injected should range between 15 and 30 cc., but no more than 30 cc. should be used in any given case. The prostate is exposed suprapubically and its size is estimated. The regional lymph nodes are examined for metastases. The radioactive material is deposited in each fascial compartment by separate injections as illustrated in this article. The proper distribution requires care and considerable experience. The duty of the radiologist is to consult with the surgeon regarding the dosage to be used, to prepare the colloidal gold solution and to develop and maintain protective measures against radioactive exposure to personnel.

Follow-up studies have shown negative biopsies in a significant number of patients following treatment of this type. Clinical arrest has been obtained in 48 of 100 cases. With improvement in technique the incidence of complications has been tremendously decreased. In the first 50 cases 24 complications occurred. In the second 50 cases only 4 complications of a minor nature were observed.

Secondary injections through a perineally placed needle are of value for the destruction of nodules which are not completely destroyed by the first operation. This procedure should not be done earlier than three months after the preliminary injection.—*George W. Chamberlin, M.D.*

COWAN, IRVING I., CRON, ROLAND S., BURGESS, GORDON F., and KARIORIS, FRANK G. Transport of radioactive colloidal gold between serous cavities. *Surg., Gynec. & Obst.*, June, 1954, *98*, 721–724.

This case is reported because of the interest in the dynamics of the so-called Meig's syndrome and the many conjectures concerning coexistant hydrothorax and ascites.

There was a rapid transport of radioactive gold (Au^{198}) from the peritoneal cavity to the pleural space in a case of liposarcoma of mesenteric fat with extensive ascites and bilateral pleural effusion. The maximum concentration in the pleural fluid was present within two hours. Radioactive gold was found in the abdominal cavity following right pleural space administration with a maximum concentration in one hour. Very little therapeutic effect was noted from this type of radioactive gold treatment. The concentration of the transported Au^{198} was found to be ten times greater in the cell mass than in the supernatant fluid. The differences in concentration of the gold in other body fluids, *e.g.*, blood, urine, feces, did not indicate the blood stream as carrier.

Some form of rapid transdiaphragmatic lymphatic transport appears as the most plausible explanation for the results obtained in this study.—*Chauncey N. Borman, M.D.*

MÜLLER, J. H. Bisherige Erfahrungen mit der intraperitonäalen und intrapleuralen Applikation von künstlich radioaktiven Isotopen (Zn^{63}, Au^{198}) für die Behandlung der vom Ovar ausgehenden Karzinosen, seit 1945. (Experiences with intraperitoneal and intrapleural application of radioactive isotopes [Zn^{63}, Au^{198}] in the treatment of carcinosis arising from the ovary, since 1945.) *Schweiz. med. Wchnschr.*, May 1, 1954, *84*, 509–510.

The author introduced the treatment with intraperitoneal injections of radioisotopes in 1945. He started out with suspensions of Zn^{63}, abandoned it after four years in favor of colloidal Au^{198}, and was also the first to use radiogold intrapleurally in 1949. Since 1950, in addition to surgery and/or roentgen and radium therapy, intraperitoneal administration of Au^{198} is part of the routine treatment of carcinoma of the ovary at the gynecologic Clinic of the University of Zürich, of which Müller is the radiotherapist and histopathologist. Müller reported on this subject at the International Radiological Congress in Copenhagen in July, 1953, and again in September, 1953, as a guest speaker at Oak Ridge.

Sixty-nine cases are classified as follows: (1) 15 had radical surgery, without evidence of metastasis at operation; 50–225 mc. Au^{198} were introduced into an artificially created hydro-(pneumo-)peritoneum; so

far (1½-3 years) all (100 per cent) are asymptomatic. (2) Ten had also radical surgery, though including partial or total removal of peritoneal metastases; 80–400 mc. were administered fractionally, never exceeding 150 mc. at one time; 8 (80 per cent) are alive (up to 2½ years) and free of symptoms. (3) Sixteen underwent partial surgery, because of extension beyond the pelvis; 45-225 mc. were given as above described; 7 (44 per cent) survive (½–4 years), clinically free of disease. All these 41 cases, and some from the next two groups, received also "systematic" roentgen and radium therapy, not further detailed in the text. During exploratory laparotomy, (4) 22 and (5) 6 patients were found to have far advanced carcinomatosis with liver and other metastases; ascites were present in both groups, pleural effusion in the last; palliation could be obtained in 65 per cent of them with 90–560 mc. Au^{198} intraperitoneally and/or 40–225 mc. intrapleurally; 5 are still alive (1–2½ years), even if progressively deteriorating.

The penetration of lymphatic channels by radiogold is considered a "functional and selective" process of definite advantage in this "very acceptable method of treatment."—*E. R. N. Grigg, M.D.*

Mayor, G. Le radiocobalt dans le traitement des tumeurs malignes de la vessie. (The radiocobalt in the treatment of malignant tumors of the bladder.) *Schweiz. med. Wchnschr.*, May 1, 1954, *84*, 510–512.

A latex container, resembling the oversized bulb of a retention catheter, is inserted through the urethra into the bladder and filled with a colored fluid to detect eventual leakage. After several hours, the fluid is replaced with a radioactive solution of Co^{60} chloride. The urine, evacuated through the indwelling catheter, is regularly checked for radioactivity (leakage). Once the balloon had to be withdrawn ahead of time because of massive hemorrhage obstructing the catheter, and in another case for severe tenesmus. In 2 patients the bag ruptured while being filled, which was remedied by immediate evacuation and irrigation of the bladder. Failure to discover this accident at once is dangerous because the resorbed Co^{60} will accumulate in the liver and bone marrow.

The scarce physical details indicate that the latex container stops the soft radiation, while the "optimal distance of therapeutic efficacy of radiocobalt is 8–12 mm." Sixty cubic centimeters of "solution" were left in the bladder for 8–10 days. The "total" dose, less than 9,000 r at first, was later increased to 11,000–12,000 r. Accurate technical data are essential for reproducibility.

The method is mainly recommended for malignant papillomatosis and other superficial tumors. Exophytic growths must be removed by endoscopy or even suprapubic approach, prior to application of radiocobalt. Once the carcinoma has infiltrated deeply into the bladder wall, radical surgery is required, including transplantation of the ureters, with routine postoperative irradiation from megavoltage sources.

In most of the 60 cases treated, cessation of hematuria was one of the immediate results, although in 11 patients it persisted intermittently. The series as a whole was not too favorable, as the method was applied in 50 patients only for the control of recurrences following surgery. From the total, 17 (28 per cent) died: 11 by generalized metastases; 1 after cystectomy; 1, locally cured, by supervening, metastasized prostatic carcinoma; and 4 by intercurrent cardiac ailments. Improvement was noted in 21 (35 per cent), even if 6 of them showed local recurrence; 15 had prolonged cystitis, while 8 revealed alterations of the vesical mucosa interpreted as radionecrosis, very slow in improving under conservative management. Excellent results were obtained in 22 (37 per cent) patients, who had no cystoscopic evidence of disease after up to three years of observation.—*E. R. N. Grigg, M.D.*

Clark, Herbert M. The occurrence of an unusually high-level radioactive rainout in the area of Troy, N. Y. *Science*, May 7, 1954, *119*, 619–622.

This is a report of a study made in Troy, N. Y., by the Department of Chemistry of the Rensselaer Polytechnic Institute. On April 25, 1953, at 8:30 A.M., EDT, the seventh nuclear bomb in the spring series was detonated from a 300 foot tower at the Nevada proving ground. Thirty-six hours later, an unusually violent electrical storm occurred at Troy —2,300 miles from the proving ground. It flooded streets and cellars, and caused heavy damage. But it was unusual in another respect in that it had left in its wake an exceptionally high, though not hazardous, deposition of radioactive material. This became evident on the day following the storm when the background rates were determined for the G-M counters in the radiochemistry laboratory at Rensselaer Polytechnic Institute. The background rate for the shielded G-M counter nearest the outside wall of the counting room was observed to be more than 3 times greater than the normal rate of about 30 counts/minute. Outside the building, it was observed that the level of beta and gamma radiation on the pavement, sidewalks, soil, etc., was great enough to be readily measured with portable radiation survey meters. It thus became evident that the extent of the rainout was much greater than that detected in the area from any previous nuclear detonation. The contamination per square foot was comparable with that reported by Eisenbud and Harley for fallout from the 1952 tests as settled dust at stations in Utah and Nevada in the 200 to 500 mile annulus around the test site. During the first day after arrival, the activity of drinking water at Troy was about 100 to 1,000 times greater than the natural radioactivity generally associated with surface and ground water.

Charts and tables are included, illustrating the findings, water samplings, etc.; also radioautographs of a leaf and a piece of asphalt shingle, showing the presence of fission products. These were obtained by placing Eastman No-Screen Medical X-ray film in contact with the objects tested.—*D. S. Kellogg, M.D.*

Davis, Loyal, and Craigmile, Thomas. Results of radioactive isotope encephalography in patients with verified intracranial tumors. *J. Neurosurg.*, May, 1954, *11*, 262–267.

The authors review the results of isotope encephalography, performed after the administration of radioactive di-iodo-fluorescein or radioactive sodium iodide, in 200 patients with verified primary or metastatic intracranial tumors. Primary intracranial tumors were found in 174 cases while metastatic lesions were encountered in 26 instances.

Analysis of the results using di-iodo-fluorescein in the greater number of cases initially and sodium iodide in fewer instances later in the series, revealed a slightly higher incidence of accurate findings with the use of di-iodo-fluroescein. A detailed analysis of the percentage uptake by the various neoplasms encountered in this study is also presented.

In individuals with primary intracranial tumors, encephalography with di-iodo-fluorescein resulted in accurate localization of the lesion in 61.6 per cent of the patients examined. Radioactive sodium iodide gave a precise localization of the neoplasm in 52.8 per cent of all patients examined by that method. In 21 patients with metastatic intracranial tumors, di-iodo-fluorescein showed evidence of the presence of an organic lesion in approximately 76 per cent, and precise localization of a solitary metastatic nodule was obtained in 47.6 per cent of the cases.

Examination following injection of radioactive sodium iodide in 5 individuals with metastatic lesions was discouraging. One patient with a solitary nodule displayed a generalized increase in radioactivity without evidence of focal concentration. Four other patients examined by the same method showed no abnormalities in their tracings.—*William H. Smith, M.D.*

Watson, T. A., Johns, H. E., and Burkell, C. C. The Saskatchewan 1,000-curie cobalt 60 unit. *Radiology*, Feb. 1954, *62*, 165–176.

The authors outline their experience with the cobalt 60 unit used in their institution on a routine rather than an experimental basis for the past year. A comparison is made, from purely physical aspects, between the energy produced by this unit and that produced by conventional and very high voltage roentgen units.

For practical purposes the beam from the cobalt unit can be considered monochromatic. In this respect it is very different from radiation generated by roentgen machines operating at 200 kv., 3 mev., or 25 mev., which produce a continuous spectrum of radiation. From a consideration of spectral distributions of these various radiations it is seen that the average energy of the radiation produced with a peak energy of 3 mev. is quite similar to that from cobalt, while betatron radiation is more penetrating and that of 200 kv. is much less penetrating.

In considering the distribution of electrons from the above mentioned sources it is seen that the spectrum of electrons from cobalt is not unlike that of the other radiations, and, thus, no special effects are to be expected from cobalt because of its monoenergetic beam. Ion density of an electron tract is important in determining biological effect. Comparing the ion density spectra of these various radiations it is seen that they are very similar for cobalt, 3 mev., and betatron radiation, but are quite different from 200 kv. radiation. This may explain the difference in therapeutic dosage levels required for 200 kv. as compared to the higher energy radiation.

The percentage depth dose produced in a water phantom was compared for the various sources. Marked differences for the first few centimeters below the phantom surface were encountered. The surface dose for betatron radiation is about 15 per cent and rises to 100 per cent at a depth of 4 to 5 cm. whereas the surface dose of cobalt is between 30 and 40 per cent, rising rapidly to 100 per cent at 5 mm. Side scatter for 200 kv. is much more marked than for either cobalt or betatron radiation, and, of course, the depth dose is much lower.

The advantage of using either cobalt or betatron radiation in regions where bone or cartilage is involved is obvious when it is realized that with higher energies the differential absorption of these structures, compared with soft tissues, is almost at a minimum.

From a clinical standpoint the cobalt unit is considered to be indicated particularly for deep-seated tumors and tumors adjacent to bone and cartilage. Rotational therapy does not appear to offer any advantage over small field beam directed technique at this energy.—*Michael J. Healy, M.D.*

Untermyer, S. Portable thulium x-ray unit. I. The portable unit. *Nucleonics*, May, 1954, *12*, 35–36.

The Argonne National Laboratory and the Army Medical Research Laboratory have developed a simple portable radiographic unit for use in isolated locations where conventional bulky roentgen-ray equipment is not available. The source of radiation is thulium-170 with a half-life of 129 days. Its radiation energy spectrum is comparable to that of an 80 kv. roentgen-ray apparatus. Its radiations fall in the region of maximum photographic effect on the roentgenographic film. The radiations have a penetrating power comparable to those from a 100 kv.

roentgen tube. Thulium has only recently become available in metallic form at reasonable cost. Although no definite price has been set by the AEC for radiothulium, it is estimated that the amount used in the unit would cost about one hundred and seventy dollars.

The unit consists of an aluminum capsule containing a 200 mg. source of radiothulium suitably shielded by 1 inch of lead. The whole unit weighs about 7 pounds. The dose rate at the surface of the unit is approximately 75 r per hour. The unit can be used for radiography of the extremities, for inspection of thin castings and for the measurement of the density or height of liquids.—*Leslie K. Sycamore, M.D.*

Spedding, F. H., Daane, A. H., and Powell, J. E. Portable thulium x-ray unit. II. Methods for preparing thulium oxide or metal. *Nucleonics*, May, 1954, *12*, 37.

Thulium is one of the rarest of the rare earths occurring in a number of rare-earth ores, the best of which is gadolinite, a dense black silicate rock.

In preparation of the metal the ore is treated with strong nitric acid which is then reduced in concentration by boiling and dilution. The rare earths are precipitated as oxalates, ignited to oxide, and then dissolved in hydrochloric acid. The heavy rare earths are separated out by treating with ethylenediaminetetraacetic acid and pouring the mixture through a bed of ion-exchange resin and then the components separated by a similar method. The thulium oxide obtained is converted to the fluoride and reduced with calcium in an argon atmosphere to give the pure metal. The commercial price is estimated to be somewhere between five dollars and one hundred dollars per gram.—*Leslie K. Sycamore, M.D.*

Hasterlik, Robert J. Portable thulium x-ray unit. III. Clinical radiography with a Tm^{170} source. *Nucleonics*, May, 1954, *12*, 37.

Radiographs of the hand and wrist can be obtained by using a lead-backed cassette with mid-speed screens at a 15 inch source-object distance with an exposure time of thirty seconds.

A thulium source with an anticipated dose rate at least four times greater is now in preparation, and by using this with high-speed screens it is expected that radiography of the extremities can be accomplished with an exposure time of one to three seconds. —*Leslie K. Sycamore, M.D.*

Østling, G., and Tøtterman, G. Extrinsic (P^{32})/intrinsic (P^{31}) phosphorus clearance ratio in man. *Scandinav. J. Clin. & Lab. Investig.*, 1954, *6*, 25–27.

The renal clearance of intravenously infused radiophosphorus was determined in 11 surgical patients with normal kidney function. To maintain a constant blood level of radioactivity, 4–6 μc. of radiophosphorus as sodium phosphate in an initial injection was followed by a continuous infusion of the same solution at the rate of 0.33 μc. per minute. The specific activities of the blood phosphorus and urine phosphorus were determined between 15 and 25, 25 and 35, and 35 and 45 minutes after the initial injection.

The results confirmed previous reports that the specific activity (ratio of radioactive infused phosphorus to the stable intrinsic phosphorus) of the urine was consistently higher than that of the plasma at each time interval studied. This would indicate that the infused phosphate is more readily excreted than the inherent serum phosphate. It is postulated that the intrinsic plasma phosphate is bound in a physicochemical state which is different from that of the newly introduced phosphate.—*R. Kenneth Loeffler, M.D.*

Rugh, Roberts, and Booth, Elisabeth. Modification of maternal and fetal effects of radioiodine by pretreatment of the mother. *J. Pediat.*, May, 1954, *44*, 516–533.

The authors conducted experiments to determine if thiouracil, methimazole or thyrotrophic hormone treatment of a pregnant mouse protect the offspring against the expected radioiodine damage to their thyroid glands when it is injected into the mother. The study included determination of retained radioactivity at various time intervals as well as measurements of the thyroid gland size and histologic analysis at two months of both mother and offspring.

Pretreatment with larger amounts of thyrotrophic hormone caused the pregnant mouse to retain more of the radioiodine while both thiouracil and methimazole caused the pregnant mouse to excrete more of the radioiodine than the pregnant controls.

When litters were considered as units, regardless of their size, those from thiouracil-protected mothers received a smaller portion of the available radioiodine than was retained by the mother. The ratio was about 3 to 1 as compared to 1 to 1 for the control group. Thus thiouracil definitely protected the fetal thyroids. Methimazole had a similar but lesser effect.

A single injection of 100 μc. of I^{131} to the pregnant mouse on the eighteenth gestation day is sufficient to reduce the size of the maternal and fetal thyroid, two months later, by at least 20 per cent.

Histologically, thiouracil also definitely protected both the maternal and fetal thyroids against radioiodine-induced necrosis. Methimazole had a similar but lesser protective effect.

It was found that the effects of thiouracil, methimazole or thyrotrophic hormone were direct but brief and transient while the necrotic effect of radio-

iodine was slow to be realized. The drugs were used prior to radioiodine injection and did modify the radiation damage to both the maternal and fetal thyroids. The authors suggest further study to determine if additional protection of the thyroids might be achieved by post-irradiation injection of thiouracil.—*Geno DiBagno, M.D.*

Kyker, Granvil C. Biochemical consideration of distribution. *Am. J. M. Sc.*, May, 1954, *227*, 572–589.

The article is a well written and excellently illustrated discussion, and emphasizes several important factors in the field of radioisotopes. To quote the author: "There are several well established factors known to influence prominently the metabolic pattern of distribution of internally administered radioisotopes."

The paper deals with the problems of administration, collection, and localization, and elimination of various radioisotopes. The future potential of many isotopes, which are now being used, is largely obscure, since the full details of the above problems have not been completely worked out. It is certain that other and newer isotopes will be offered in the near future, and will arouse considerable interest in the medical profession. There are many factors which affect the distribution of administered isotopes, and this field in general remains an unsolved problem. The author stresses the importance of extensive information and experimentation in animals prior to the use of any radioisotopes in therapeutic or diagnostic medicine.

A point which is of great interest is the use of yttrium 90 in the chloride state, and in an unbuffered solution, as a method of localization. It was found that this preparation, in the unbuffered state, with sufficient carrier, would be converted instantly into an immobile form by the buffered tissue fluids. A table of the results of using this substance is included in the article, and shows that intraplurally administered yttrium suffered a loss of only 1.71 per cent of the total dose from the chest cavity after 186 hours. Other types of injection were carried out, including intramuscular, intraperitoneal, and subcutaneous, and similar localizing or non-absorbing figures were obtained.

Another point of great interest to radiologists and radiophysicists is a substance which is referred to as EDTA. This subtance has been shown to have some practical phases, which present the possibility of decontamination of an individual of a radioactive isotope after administration of a therapeutic or diagnostic dose. The substance (EDTA) has presented some promise in this highly complex field. It offers the prospect that a patient may be administered a dose of a radioisotope and, when the appropriate therapeutic time has lapsed, the substance may be used in decontamination of the patient.

The author uses throughout the article excellent charts and graphs, and constantly emphasizes that a great many factors in this field of distribution are still largely unknown, but that some progress is being made.—*O. M. Richardson, M.D.*

Peirce, Carleton B. The known and potential value of radioactive isotopes as therapeutic agents. Gordon E. Richards Memorial Lecture. *J. Canad. A. Radiologists*, March, 1954, *5*, 1–10.

The second Gordon E. Richards Memorial Lecture is a well conceived review of the therapeutic uses of radioactive isotopes. It is stated that to be useful and practical, an isotope should either be (1) more plentiful, versatile, and powerful and have fewer side effects than the agent previously employed or (2) be able to be utilized for a new procedure by virtue of its unique properties. It is stressed that the criteria of biochemical, pharmacologic and physical characteristics are of great import.

A brief résumé of the external, interstitial, intracavitary, and parenteral methods of use is given together with descriptions of the physical properties of the isotopes that are most widely employed at present.—*George Roberts, M.D.*

Halmi, N. S., and Gude, W. D. The morphogenesis of pituitary tumors induced by radiothyroidectomy in the mouse and the effects of their transplantation on the pituitary body of the host. *Am. J. Path.*, May-June, 1954, *30*, 403–419.

This study deals with the changes which are encountered in the pituitary bodies of mice at various intervals after destruction of the thyroid gland and with the alterations which can be seen in the hypophyses of radiothyroidectomized and normal mice bearing transplanted pituitary tumors.

The most drastic early changes subsequent to the administration of thyroid-destructive doses of I^{131} occurred in the beta cells. As early as ten days after radiothyroidectomy their aldehyde fuchsin-staining (beta) granules were completely absent and they were transformed into thyroidectomy cells. The delta cells showed no alterations this early, but after sixty days appeared distinctly enlarged and very heavily granulated. The only marked difference in the late changes, after 120 to 150 days, was the presence of a large number of cells which appeared to be hypertrophic delta cells.

Adenomatous nodules appeared in the pituitary bodies at about six to ten months after radiothyroidectomy. The parenchyma between the nodules showed the previously described thyroidectomy changes. In the mice with greatly enlarged pituitary bodies, ten months or more after administration of I^{131}, the bulk of the organ was occupied by neo-

plastic tissue. The tumor cells were usually quite uniform and but few mitotic figures were encountered.

The pituitary bodies bearing dependent or autonomous transplanted tumors, 150 to 300 days after the host had been radiothyroidectomized, all showed thyroidectomy changes and most of them contained adenomas. Two of the seven female mice in this group showed histologic criteria of malignancy, with tremendous nuclear polymorphism, multinucleated cells, a great number of mitotic figures, and infiltrative growth as indicated by the presence of acidophils amidst tumor cells and by the invasion of the sellar periosteum by the neoplasm.

The most striking change in the pituitary bodies of normal hosts bearing large autonomous grafts was the diminution in the size of the acidophils. The beta cells were definitely and sometimes almost completely degranulated, and were invaribaly reduced in size. The delta cells appeared somewhat sparser than in normal controls.

The significance of these findings in the histophysiology of the pituitary body of the mouse is discussed. Several photomicrographs are included.—*D. S. Kellogg, M.D.*

Berg, Harold F., Isaacs, Avrom M., and Christophersen, William M. Localization of radioactivity in the urinary bladder and the regional lymph nodes. *J. Urol.*, Sept., 1954, *72*, 382–388.

The mortality rate from infiltrating bladder cancer is very high and no method of treatment up to the present time has proved very satisfactory. This type of cancer spreads principally to the external iliac, hypogastric and common iliac lymph nodes.

The authors report their results with animal experiments, designed to offer a method of delivering effective irradiation to the bladder tumor and its lymphatic drainage. After exposing the urinary bladder of dogs, they injected 5 millicuries of radioactive colloidal gold in 5 cc. of normal saline solution to which had been added 300 turbidity units of hyaluronidase. The dogs were sacrificed at intervals of from five to fifteen days after injection and the radioactivity of the tissue was measured with an end window Geiger tube.

A high concentration of radioactivity was found at the site of injection in all 12 dogs. A consistent and fairly high level of activity was noted in the lymph nodes draining the urinary bladder. Very low radioactivity was present in the liver and spleen.

The pathological changes, associated with the injection, are also described. There was some necrosis at the injection site; fibroblastic proliferation was present adjacent to the site of the injection; a thin layer of fibrin appeared on the peritoneal surface and there was some swelling of the transitional cells of the mucosa.

The results of these experiments suggest the possibility of a clinical trial in patients with inoperable bladder carcinoma. Palliation may be expected if a sufficiently large amount of isotope for effective irradiation has been injected.—*George W. Chamberlin, M.D.*

Bulkley, George J., Cooper, John A., and O'Conor, Vincent J. Intraprostatic injections of radioactive colloids: II. Distribution within the prostate and tissue changes following injection in the dog. *J. Urol.*, Sept., 1954, *72*, 476–484.

This article gives a detailed discussion of the histopathological changes which follow the interstitial injection of radioactive material into the prostatic gland of normal dogs. Ten dogs were injected with colloidal chromic phosphate and 9 with colloidal gold. The animals were sacrificed at intervals of from two weeks to three months in the case of phosphorus, and one week to seven weeks in the case of gold. All organs were examined grossly and microscopically. Tissues were prepared in the usual way, using paraffin embedding for sectioning and were stained with hematoxylin and eosin. The prostates injected with gold were also stained by the method of Elftman and Elftman in order to visualize the colloidal particles. Serial sections of the prostates were made to determine the distribution of colloid.

The animals injected with radioactive colloidal chromic phosphate showed no gross or microscopic abnormalities excepting those which were present in the prostate gland itself. The regional lymph nodes were grossly unchanged and exhibited little, if any, radiation reaction.

The prostate showed areas of subcapsular hemorrhage at two to five weeks. Serial sections of the gland revealed that the material had not been distributed uniformly throughout the tissue and that large areas of the gland were completely free of change. This was true in all of the prostates examined in spite of efforts to reach every part of the gland by the injecting needle. The microscopic reaction to radiophosphorus consisted of the early changes of acute necrosis, hemorrhage and slight exudative reaction. The necrosis involved both fibrous and connective tissue as well as epithelial elements. The blood vessels showed a proliferative arteritis with necrosis of the wall. The acute reaction subsided after five to six weeks and healing became fairly complete at the end of three months. At this time there were increased connective tissue, decreased or absent glands, cystic dilatation of some glands and in some areas hyalinization. Normal glandular structures were found in the center of areas of hyalinization in several cases.

The animals injected with radioactive colloidal gold showed much more marked periprostatic reaction as well as radiation effect in the regional lymph

nodes. The dogs which were sacrificed at the end of one and two weeks showed edema of the periprostatic fat and enlarged hemorrhagic iliac lymph nodes. By the end of seven weeks, there were firm fibrous adhesions involving the prostate. The serial sections showed about the same patchy pattern of distribution as was observed in the case of radioactive phosphorus. Microscopically, the appearance after the injection of radioactive gold was quite different from that after the injection of radioactive phosphorus. Sections of the prostate removed at one and two weeks after injection of radiogold showed an acute suppurative reaction with exudate in the glands and connective tissue. There were only small areas of hemorrhage and necrosis. The suppurative appearance was at first thought to be due to a bacterial prostatitis, but since all dogs in this group were affected similarly, it was decided that this was due to the radiation reaction. The late microscopic findings were similar to those seen after the injection of radioactive phosphorus. There was scar formation with increased connective tissue and the glands were completely destroyed in some areas and only partially destroyed or not affected in other areas. It was estimated that from 15 to 75 per cent of the total functioning prostatic tissue was destroyed in the animals included in this experiment, but complete destruction of tissue was not accomplished in any animal.

Further efforts should be made to improve the technique or the composition of the material used in order to secure a more complete distribution of the colloidal particles throughout the prostate gland.—*George W. Chamberlin, M.D.*

Root, Samuel W., Tyor, Malcolm P., Andrews, Gould A., and Kniseley, Ralph M. Distribution of colloidal radioactive chromic phosphate after intracavitary administration. *Radiology*, Aug., 1954, *63*, 251–259.

Preliminary studies indicate that the distribution of chromic phosphate after intracavitary injection is similar in most respects to that of radioactive colloidal gold. The information presented is based on only a small number of patients, but the results seem fairly consistent. There is good evidence that after the injection of chromic phosphate most of the radioactivity remains on the walls of the injected cavity. Only a small percentage of the injected dose is present in the blood at any one time, but it is a larger proportion of the dose than is seen after injection of gold-198.

There is evidence that some of the radioactive phosphorus does break away from the colloid complex to be distributed in the body like phosphate ion. Three points of interest in which the behavior of the chromic phosphate differs from that of gold-198 after its intracavitary injection are the high concentration of the radioactivity in the red blood cells, the higher urinary excretion, and the greater deposition in neoplastic tissues. Approximately 5 per cent of the administered dose is excreted in the urine over a period of eleven days.

From the point of view of distribution, chromic phosphate appears to be suitable for intracavitary therapeutic use.—*Arno W. Sommer, M.D.*

Rusche, Carl, and Jaffe, Henry L. Treatment of prostatic carcinoma with radioactive colloidal chromic phosphate (P^{32}): a preliminary report. *J. Urol.*, Sept., 1954, *72*, 466–475.

Radioactive colloidal chromic phosphate has a half-life of 14.3 days. It is an emitter of pure beta rays with an energy of 0.7 mev. which have a range of 8 mm. of maximum penetration in water or tissue.

The shielding required to protect a surgeon's hands is minimal since the beta rays are easily filtered out by plastic, glass or aluminum. The rubber gloves worn by the operator are sufficient to protect the skin of his hands from contact with beta rays. If there is any contamination of instruments, linen, operating room table or floor, the radioactive material may easily be washed off by means of a detergent and water. There is no problem with the handling of the postoperative patient since no gamma irradiation is involved. Due to the fact that the effect of the beta particles is localized, it is at least theoretically possible to destroy all cancer tissue without injuring the adjacent normal tissues. It is questionable whether the material is taken up by the lymphatics and delivered to the regional lymph nodes as has been demonstrated with radioactive gold.

In this article, a report is made of the clinical results of treatment of 28 patients with carcinoma of the prostate, who had been injected with colloidal chromic phosphate. The procedure consists of a cystotomy and the removal of as large an amount of prostatic tissue as can be done transvesically. The consistency and size of the remaining prostate is then estimated by a bimanual palpation with one finger in the rectum. Multiple 21 caliber spinal puncture needles are inserted into the substance of the prostate, seminal vesicles, periprostatic tissues, and involved regional lymph nodes. The solution injected contains from 1 to 3 millicuries of chromic phosphate per 1 cc. along with hyaluronidase and epinephrine. Approximately 0.3 to 0.5 mc. is injected for each gram of tissue. The largest amount injected in any single case was 40 m.c.

In 14 of the patients, there was a remarkable decrease in the size and a definite change in the consistency of the prostate gland within thirty to sixty days following treatment. Fifteen patients experienced a gain in weight and general feeling of well being. In 2 patients osseous metastases developed following treatment, in one after six months and the other after four months respectively.

The microscopic findings after treatment were not

as striking or as encouraging as the rectal and clinical findings. In all of the biopsies, which were taken by a perineal needle three months after treatment, there was still evidence of tumor being present. Marked scarring, necrosis and diffuse fibrosis with the cellular changes which were observed at the site of the implantation of the radioactive material, suggested that more thorough dispersion of the radioactive chromic phosphate might have produced complete destruction of the prostatic cancer.

There were no serious complications. Some of the patients had rectal irritation and all of them had mild bladder symptoms, which subsided in thirty to forty days. There was no evidence of depression of the bone marrow and no evidence of radioactivity in the spleen, kidneys or lungs.—*George W. Chamberlin, M.D.*

Schultz, Alvin L., Sandhaus, Sol, Demorest, Howard L., and Zieve, Leslie. Clinical value of the plasma butanol-extractable (thyroxine) I^{131} in the diagnosis of hyperthyroidism and myxedema. *J. Clin. Endocrinol. & Metabol.*, Sept., 1954, *14*, 1062–1068.

The protein-bound iodine (PBI) of the plasma consists primarily of the hormone thyroxine, but also contains other organic iodides. Previous investigators have shown that the thyroxine fraction can be extracted from plasma with butyl alcohol. The percent of an orally administered tracer dose of radioiodine which appeared within twenty-four hours in the total plasma, in the protein-bound fraction, and in the butanol extractable fraction was determined in 50 euthyroid patients, 12 hyperthyroid patients, and 5 patients with primary myxedema. The last two values, expressed as per cent of radioiodine per liter of plasma, give an indication of the relative rate of formation of organic iodine compounds, and are not a measure of either the quantity formed per day, or of the circulating levels of these compounds. Either value, BEI^{131} (butanol extractable I^{131}) or PBI^{131}, divided by total I^{131} per liter of plasma, will give a corresponding "conversion ratio." The BEI^{131} values were consistently about 80 per cent of the PBI^{131} except in the lower ranges. With lesser radioactivity in the protein samples, the average ratio was also about 80 per cent, but with greater individual deviations attributable to the greater counting errors with lower counting rates. Since BEI^{131} is so consistently 80 per cent of the PBI^{131}, and is technically more difficult to determine, the authors conclude that the BEI^{131} assay has little clinical applicability.

For comparative purposes, basal metabolic rate and thyroid uptake determinations were carried out on each patient. Using clinical diagnosis as the criterion for evaluation, it was noted that the PBI^{131} and BEI^{131} differentiated the euthryoid patients from those with hyperthyroidism in most cases, with the euthyroid values in the narrow ranges of 0 to 0.7 and 0.5 per cent per liter respectively, while the hyperthyroid patients had values extending from 0.7 to 8, and 0.5 to 6 per cent per liter respectively, ranges about ten times as wide. The basal metabolic rate and iodine uptake value covered about equally wide ranges for either euthyroid or hyperthyroid patients, and with more overlapping. Because of these differences, the authors feel that either the PBI^{131} or BEI^{131} is a better single clinical test to differentiate euthyroid from hyperthyroid patients, than is either the basal metabolic rate or the thyroid iodine uptake. The PBI^{131} and BEI^{131} tests were of little value in differentiating euthyroidism from hypothyroidism. Similarly, either "conversion ratio" sharply differentiated hyperthyroid from euthyroid patients, but was poor for differentiating hypothyroid from euthyroid patients. —*R. Kenneth Loeffler, M.D.*

Richardson, Jasper E., Kerman, Herbert D., and Brucer, Marshall. Skin dose from a cobalt 60 teletherapy unit. *Radiology*, July, 1954, *63*, 25–36.

The main advantages of high energy radiation over low energy radiation in the treatment of deep seated tumors are: (a) an increase in percentage depth dose, (b) decrease in side-scatter, resulting in flatter isodose curves with a smaller penumbra, and (c) the establishment of electronic equilibrium at a greater depth, resulting in a smaller skin dose. Using a Co^{60} unit, the authors found that little can be done to affect (a) or (b). However, for short cone-to-skin distances, (c) is greatly affected by electrons scattered from the walls of the collimating system, and they studied the electron buildup region and the optimum cone design necessary to preserve the advantage of (c).

A detailed description of the equipment, procedure and the results is given.

Their general conclusions were that for short cone-to-skin distances, electrons from the collimating system contaminate the beam and result in an appreciable skin dose. This can be reduced by proper design of the treatment cone. Although a material of intermediate atomic number is superior as an inner lining and as a filter to remove secondary radiation, the choice of the material to be used as an electron filter is not too critical, except for contact treatment, because of the angular distribution of electrons from the materials.

For cone-to-skin distances greater than 20 cm., an electron filter is not needed. Between 4 cm. and 20 cm. cone-to-skin distance, the skin dose is reduced appreciably if an electron filter is used. At these distances, both intermediate and high Z materials were found to be superior to those of low atomic number, with little difference found between the intermediate and high Z materials. For cone-to-skin distances between 0 cm. and 4 cm., optimum results were obtained with a filter material of intermediate atomic number. The difference between intermediate

and high Z materials was most significant at 0 cm. cone-to-skin distance.—*C. L. Stevenson, M.D.*

Fischer, Konrad Peter. Die endobronchiale Radiokobalt-Anwendung. (The use of radioactive cobalt endobronchially.) *Strahlentherapie*, 1954, *94*, 374–383.

The author has employed endobronchially placed perles of radioactive cobalt in the treatment of 6 patients with bronchial carcinoma. The results have encouraged him to continue with his efforts to improve technical methods and increase tumor dose.—*Henry G. Moehring, M.D.*

Henschke, Ulrich K., James, Arthur G., and Myers, William G. Radiogold seeds in clinical radiation therapy. *Radiology*, Sept., 1954, *63*, 390–399.

Clinical experience in the first 100 patients treated by the authors with radiogold seeds has shown that these seeds can be used successfully as replacement for radon seeds. The simplicity of protection and the ease of preparation of radiogold seeds of uniform strength are advantageous. No appreciable differences in therapeutic response were observed as compared with radon, radiocobalt, and radium.

Four methods of application of radiogold sources were used: (1) molds; (2) intracavity applicators; (3) permanent implants; (4) removable nylon implants.

Radiogold offers certain advantages over other gamma emitters: (1) the radioactive substance does not need to be recovered after the completion of the treatment; (2) effective protection of adjacent tissues by a lead shield is accomplished very easily; (3) hospitalization of the patient throughout the entire course of treatment is not absolutely necessary.

Radiogold seeds in removable nylon applicators are preferred over needles since they permit more accurate implantation, better individualization of treatment, more comfort to the patient, and decreased exposure to the operating personnel.—*A. W. Sommer, M.D.*

Remold, F., Siegert, A., and Stamm, H. Das radioaktive Gold Au^{198} bei der Behandlung von Ovarialkarzinomen, Peritoneal- und Pleurakarzinosen. (Treatment of peritoneal and pleural carcinomatosis from ovarian carcinoma with radioactive gold, Au^{198}.) *Strahlentherapie*, 1954, *94*, 367–373.

Eleven patients with peritoneal and pleural carcinomatosis from ovarian carcinoma were treated by intraperitoneal or intrapleural injections of radioactive gold. Excess fluid was first aspirated and then doses of 31–168 mc. were administered in from 1–3 injections. Subjectively the patients tolerated the treatment well. Regression of the ascites occurred in only one patient. Tumor growth remained uninfluenced in all patients, and the general condition of the patients steadily deteriorated.

The employment of radioactive gold in the treatment of peritoneal and pleural carcinomatosis appears justified, particularly because of its promise of being effective against micro-metastatic nodules.—*Henry G. Moehring, M.D.*

CHEMOTHERAPY

Lockhart, Jean D., and Burke, Frederic G. Myositis ossificans progressiva; report of a case treated with corticotropin (ACTH). *A.M.A. Am. J. Dis. Child.*, May, 1954, *87*, 626–635.

Myositis ossificans progressiva is a rare disease characterized by the formation of areas of calcification in the interstitial connective tissue of muscles, tendons, ligaments, fasciae, and aponeuroses. The paper gives a review of the literature and is illustrated with roentgenographic reproductions and clinical pictures of the patient.

The incidence of the disease as taken from the literature indicates that it is rare. It has been reported to affect males more than females. Three stages of the lesions of the disease are described. In the first stage, lasting from hours to days, there is a doughy swelling of soft tissue, consisting of cyst-like masses over various parts of the body, but most commonly in the cervical and dorsal region, which may be hot and tender. Histopathologically, there is edema of muscle and tendon fibers, with round-cell infiltration. These lesions may drain a whitish calcific material. In the second stage, lasting for weeks, there is induration of the muscle and the pain may subside. On section, granulation tissue has replaced the larger inflammatory areas, and the muscle fibers degenerate as leukocytic infiltration continues. Osteoid tissue trabeculae are now seen in the granulation tissue. Islands of cartilage may be found within the ossifying mass intermingled with fibrous tissue. The final stage is true ossification, with bony trabeculae spreading outward from the central lesion. The lesions of the progressive form cannot be distinguished from the circumscript form of myositis ossificans. The end result of this process is a continuous band of bone from occiput to pelvis with generalized ankyloses and synostoses. The disease is relentlessly progressive, with periodic exacerbations, but survival to old age may occur, provided there is little or no involvement of the muscles of respiration and deglutition. As the vital capacity diminishes, the danger of intercurrent pulmonary infection grows. The ultimate outcome is almost complete immobility of large muscle groups.

A rounded facies of the patients with the disease is often seen. Congenital anomalies which may accompany it are absence of a phalanx, webbing of the

toes, and ankylosis of an interphalangeal joint. Microdactyly of the first great toe is also encountered.

In the differential diagnosis of the case reported, the torticollis and the ossification and ankylosis between the second and sixth cervical vertebrae, with ossification of the nuchal ligaments in this area, were somewhat suggestive of the Klippel-Feil syndrome. In its final stages, the disease is unmistakable.

The patient, a girl nine years old, was treated with corticotropin. The authors state that beneficial results may be obtained with adrenal cortex drugs in the acute inflammatory stages of this disabling disease. While it appears impractical from a medical as well as a financial aspect to maintain a patient permanently on either cortisone or corticotropin, these drugs may be held in reserve for the periodic exacerbations with hope of preventing some of the crippling end-results.—*Ralph S. Bromer, M.D.*

Grebe, Alfred A. Monostotic coccidioidal infection; report of a case successfully treated with 2-hydroxystilbamidine. *J. Bone & Joint Surg.*, July, 1954, *36-A*, 859–862.

Infections due to *Coccidioides immitis* have been classified as initial or primary infections which run a self-limited course and are nearly always focalized in the lungs; and as progressive, secondary, or disseminated infections. When dissemination occurs, the outcome is usually disastrous. To the present time there has been no known therapeutic agent which would alter the course of the disease and, once dissemination occurred, the usual result was death or, if dissemination was not too widespread, amputation of the involved part.

The purpose of the author in this article is to present a case of monostotic coccidioidal infection which did not respond to repeated wide excision of the bone lesion, but which did show rapid and apparently complete healing when treated with 2-hydroxystilbamidine. The patient was a colored male soldier, twenty-one years old, with a lesion in the left calcaneus. Roentgenograms of the os calcis showed an area of destruction in the posterior portion of the bone. After several operations for excision of the involved bone 2-hydroxystilbamidine injections were made. The diagnosis was confirmed by culture of material removed at operation and recovery of organism from the growth. After the last injection the patient was kept under observation without treatment for approximately six months, during which time laboratory tests for liver and kidney function and complement-fixation tests were repeatedly performed. No evidence of visceral damage from the drug was demonstrated and a continued reduction in titer in the serological tests was noted. No further evidence of bone destruction was demonstrated in roentgenograms. The operative wound remained healed. The patient had no complaints of discomfort and was able to walk long distances with no more than a barely perceptible limp.

A longer follow-up is desirable to obtain a true value of the treatment but the author hopes the publication of this case will stimulate further trial of the treatment.—*Ralph S. Bromer, M.D.*

Schneeberg, Norman G., Perloff, William H., and Levy, Lester M. Diagnosis of equivocal hypothyroidism, using thyrotropic hormone (TSH). *J. Clin. Endocrinol. & Metabol.*, Feb., 1954, *14*, 223–231.

This study was made to determine the value of thyrotropic hormone (TSH) in ascertaining the presence of responsive thyroid tissue in persons with equivocal, borderline or doubtful states of thyroid failure. TSH has proved to be a useful agent in differentiating primary thyroid myxedema from myxedema secondary to anterior pituitary insufficiency. In the latter, the thyroid gland is dormant but responsive to stimulation, whereas in primary thyroid myxedema there is no thyroid tissue to react.

The uptake of radioactive iodine (I^{131}) by the thyroid gland was used as a measure of the gland's function. Included in this study were 5 cases of post-thyroidectomy myxedema, 3 cretins, 14 examples spontaneous myxedema, 12 patients with hypothyroidism or myxedema secondary to pituitary insufficiency, and 24 euthyroid subjects. These were the basis for the investigation of 17 patients suspected of hypothyroidism. A tracer dose of 50 microcuries of carrier-free I^{131} was administered orally and the percentage in the thyroid gland twenty-four hours later was recorded by a Geiger counter. Approximately two weeks later this maneuver was repeated following three daily consecutive intramuscular injections of 20 to 30 mg. of TSH. The magnitude of the percentage difference between the results of the two tracer studies was accepted, for the purpose of this work, as a measure of the functioning thyroid tissue.

The TSH response was an accurate index in 16 of 17 patients studied with equivocal hypothyroidism. Thyroid medication did not inhibit the action of TSH. Repetition after as long as six months demonstrated that the results were reproducible.—*D. S. Kellogg, M.D.*

Cordiviolo, L. A., Bosq, P., and Rosselli, S. Linfogranulomatosis maligna (Hodgkin) de iniciación cutanea; remisión total con tratamiento combinado radioterapie-mostaza nitrogenada. (Malignant lymphogranulomatosis [Hodgkin's disease] of cutaneous origin; total remission with combined roentgen and nitrogen mustard therapy.) *Prensa méd. argent.*, Feb. 19, 1954, *41*, 522–525.

This is a case report of a twenty-eight year old

female patient, whose disease first manifested itself by the appearance of painless nodules behind the ear, which broke down and formed an ulceration measuring 17 by 15 cm. in diameter. Several biopsies showed the typical pattern of Hodgkin's disease, with conspicuous Sternberg cells. The patient's general condition deteriorated during the observation period; she developed fever, the spleen became palpable, and mediastinal adenopathy appeared. All involved areas were treated with roentgen therapy with fair results. A subsequent treatment with nitrogen mustard caused a complete resolution of all manifestations of the disease and the skin lesions healed. A relapse took place four months after treatment and the patient died two months later with generalized manifestations, but the skin lesions did not recur.

The authors consider Hodgkin's disease an infectious condition.—*F. Comas, M.D.*

Acree, Page W., DeCamp, Paul T., and Ochsner, Alton. Pulmonary blastomycosis; a critical analysis of medical and surgical therapies, with a report of six cases. *J. Thoracic Surg.*, Aug., 1954, *28*, 175–193.

This article deals mainly with the treatment of pulmonary blastomycosis describing the favorable results with 2-hydroxystilbamidine on the basis of a three years' experience.

Since the disease is usually quite diffuse, it is seldom amenable to surgery. The authors describe their experience with pulmonary resection in 6 cases of blastomycosis and conclude that pulmonary resection in an unsuspected and untreated case is hazardous because of the probability of spread of the disease. Occasionally, pulmonary resection of the local lesion is indicated after medical therapy. One such case is reported.—*Paul C. Olfelt, M.D.*

MISCELLANEOUS

Terrill, James G., Jr., Ingraham, Samuel C., II, and Moeller, Dade W. Radium in the healing arts and in industry. *Pub. Health Rep.*, March, 1954, *69*, 255–262.

Radium is a naturally occurring radioactive element, widely distributed in minute concentrations throughout the world. It has found widespread use in the fields of medicine and industry. Approximately 1,000 curies are being used today in the United States and it is said that the entire world supply of refined radium amounts to about 5 pounds which is approximately 2,500 grams or 2,500 curies.

Radium can be a health hazard as it exists in its natural ore, during the process in refining of the natural ore, and after it has been refined or concentrated. It can be a source of internal or external exposure potentially affecting many individuals. In the field of medicine these individuals would include nurses, technicians, therapists, radiologists, dermatologists, the patients themselves, stenographers and other persons who work in the vicinity of radiation sources. Persons who make frequent visits to radium-bearing spring waters may be subjecting themselves to chronic exposure of radium.

In the industrial field all individuals working with radium sources, such as luminous materials and radium paint and the manufacturers of many radium-containing elements, are subject to repeated exposure. Each individual is not exposed to a large amount, but radium used in industry, such as making radium dials, etc., is not sealed in a container.

The International Commission on Radiological Protection has accepted certain health standards for radium. For occupational workers the maximum permissible dose fixed in the body is 0.1 microcurie. The maximum amount of whole body external exposure permissible weekly has been set at 0.3 r, measured in air.

Exposure to radium and its decay products also occurs in mining, milling, handling and shipping of uranium, radium, vanadium, and other radioactive ores.

In view of the increased widespread use and handling of radium and its decay products in the industrial and the medical fields by increasing number of individuals, it would seem logical that official health agencies should learn where radium sources are employed in their community and should assure themselves that proper precautionary measures are maintained constantly.—*Claude D. Baker, M.D.*

Fedoruk, S. O., Johns, H. E., and Watson, T. A. An improved clinical dosimeter for the measurement of radiation. *Radiology*, Feb., 1954, *62*, 177–182.

The details of a newly designed clinical dosimeter for the measurement of radiation are given. It will instantly measure dosage rates as low as 1 r/hour with an ionization chamber volume of 0.1 cc., and this, coupled with its portability and dependability, make it very useful in radiation therapy.

The authors have been using this device particularly for measurements in roentgen-ray and radium treatment of the esophagus and pelvis. It has also been adapted for use in measuring the output of radium molds and in investigations of backscatter and depth dose.

The specific design of pelvic, esophageal, mold, stray radiation, depth dose, and isodose chambers is discussed.—*Charles L. Stevenson, M.D.*

Chanin, Martin, and Barnes, Frederick H. A chemical method for determining the activity of developer solutions. *Radiology*, July, 1954, *63*, 105–106.

Because of costly and highly technical factors in the usual methods of determining the activity of the

developer solution, the authors have developed a new method which is inexpensive and can be used by unskilled workers.

The method involves titration with the use of fresh developer solution, starch indicator solution and 0.1 normal iodine solution. By use of the formula:

$$\frac{\text{cc. (of iodine solution)} \times \text{normality (of iodine solution)}}{\text{cc. (of developer solution)}}$$

a number called the iodine value of the developer (I.V.D.) is obtained. This is constant for each brand of developer. When one determines the I.V.D. of his fresh developer solution, it is easy to check frequently his solutions and add replenisher as necessary.

Activity of the hyposolutions can be determined similarly and replenishers added as needed.—*D. N. Dysart M.D.*

Cocchi, U. Die Hartstrahltechnik in der Röntgendiagnostik. (The hard ray technique in roentgen diagnosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1954, *81*, 24–31.

The following advantages of hard ray technique (100–125 kv.) are given: (1) shorter exposure time due to increased voltage with lower amperage and lower milliampere second exposure; (2) decreased roentgen dose received by the patient; (3) elimination of unsharpness due to patient's movement; (4) prolonged tube life; and (5) less electric current expense.

As compared to the conventional 80 kv., 300–700 ma. technique, the exposure time is considerably shortened, the tube load decreased 70 to 90 per cent and the roentgen dose received by the patient decreased 50 to 78 per cent.

The best results are gained with examinations of gastrointestinal tract, spine, pelvis and skull, while examinations of the urinary tract and gallbladder are better done with the conventional technique.—*Frederick M. Reis, M.D.*

Alpen, Edward L., and Sheline, Glenn E. The combined effects of thermal burns and whole body x irradiation on survival time and mortality. *Ann. Surg.*, July, 1954, *140*, 113–118.

A large percentage of the casualties resulting from nuclear detonation will exhibit a combination of thermal burn and roentgen irradiation injury. This report deals with the combined effects of thermal burn and external whole body roentgen irradiation as compared with roentgen irradiation or thermal burn alone on mortality and survival time.

The animals (rats) were separated into four groups:

Group I—received standard burns covering varying proportions of their surface areas.

Groups II and III—received standard burns of graded areas plus whole body roentgen irradiation and whole body roentgen irradiation alone, respectively.

Group IV—served as controls, and received neither burns nor roentgen irradiation.

The authors concluded from their experiments:

(1) Animals subjected to burns without roentgen irradiation die predominantly during the first 48 hour period following trauma. This pattern is not influenced by the proportion of total body area which is burned.

(2) The median lethal burn area, LA_{50}, expressed as per cent total body area, has been determined for the initial 48 hour period.

(3) The addition of roentgen irradiation decreases the LA_{50} for the initial 48 hour period. This effect is a function of irradiation dose; the larger the roentgen radiation dose the smaller the 48 hour LA_{50}. The 48 hour LA_{50} for burn only is 33 pre cent; with the addition of 100 r, 30 per cent; with 250 r, 27 per cent; and with 500 r, 24 per cent.

(4) Roentgen radiation dosages of 100 and 250 r, which in themselves cause no mortality, in combination with burns cause deaths during the interval 4 to 30 days in excess of the total number expected from burns alone. For example, 31 to 35 per cent burns produce mortalities of 50, 65 and 100 per cent with 0, 100 and 250 r, respectively. This effect is more pronounced when using 500 r, which will produce about a 20 per cent mortality alone. With 16 to 20 per cent burns, otherwise not lethal, combined with 500 r, irradiation produces 75 per cent mortality.—*C. Peter Truog, M.D.*

Moorehead, Matthew Talmadge. A new approach to the ulcer problem: Irradiation of the surgically exposed stomach; an experimental study. *Radiology*, June, 1954, *62*, 871–874.

Experimental studies of a new method of treating peptic ulcer are presented. These studies consisted of roentgen irradiation of the surgically exposed stomach in an attempt to reduce gastric secretory activity and thereby influence the appearance of experimentally induced ulcers.

Of 18 dogs upon whom operations were performed, 7 served as controls. In 11 animals, both irradiation of the exposed stomach (1,400 to 3,000 r) and the Mann-Williamson ulcer-inducing procedure were done. In none of the 11 dogs did an ulcer develop. Irradiation in proper dosage seemed to destroy chiefly the secretory epithelium of the gastric mucosa, leaving other tissues and tunics of the gastric wall in relatively good condition.—*A. Ralph Watson, M.D.*

Haas, Lewis L., Laughlin, John S., and Harvey, Roger A. Biological effectiveness

of high-speed electron beam in man. *Radiology*, June, 1954, *62*, 845–851.

Skin tests with comparison of doses which produced seemingly similar degrees of skin erythema were done using a 17.3 mev. electron beam and a 200 kv. roentgen-ray beam. Ratios of biological effectiveness were found to be between 0.63 and 0.69.

A threshold erythema was obtained with 800 to 1,000 r of electrons while only 520 to 690 r of 200 kv. roentgen rays were required to produce a similar effect. 1,000 to 1,300 r of electrons as against 600 to 800 r of 200 kv. roentgen rays gave a standard erythema. A hypererythema was produced by 1,200 to 1,600 r of electrons while a similar effect resulted from 700 to 1,200 r of 200 kv. roentgen rays.

In therapy with different single doses and at different voltages a significantly larger physical r dose of electrons was necessary to produce similar degrees of skin reaction and tumor regression than was required with 200 kv. roentgen rays. Therapy with fractionated doses gave the same results.

Thirteen patients observed clinically showed that 10,000 and 9,500 r of electrons administered in 4½ to 5½ weeks produced more intensive skin reaction than usually follows 6,000 r of 200 kv. roentgen rays. The electron beam equivalent dose for 6,000 r of 200 kv. roentgen rays is about 8,600 r.—*Donald N. Dysart, M.D.*

O'CONNOR, J. E. A method of estimating doses in arc therapy. *Brit. J. Radiol.*, Aug., 1954, *27*, 453–458.

The author describes the construction and use of a rapid calculator for determination of the dose at any point within a body section treated by rotational irradiation. The method is applicable to any system of irradiation where the roentgen tube rotates about a patient at a uniform angular velocity while the central ray of the beam intersects the axis of rotation at right angles and the center of rotation remains a constant distance from the anode. Published depth dose tables and isodose curves for stationary fields are the basis of the computation. Depth doses may be read directly from a wheel which is designed and calibrated to rotate in proportion to the dosage rate at any point under consideration.

The accuracy of the method depends on precise centering of the beam, constant angular velocity of the tube, and sharp definition of the beam with minimum penumbra. Direct dosage distribution measurements with ionization chambers within a water-equivalent phantom agreed satisfactorily with calculated results obtained by use of this apparatus.—*Thomas B. Efford, M.D.*

VAUGHAN, JANET M., and TUTT, MARGARET L. Use of ethylene diamine tetra-acetic acid (versene) for removing fission products from the skeleton. *Lancet*, Oct. 24, 1953, *2*, 856–859.

This is a report of experimental work on young and old rabbits to determine the value of calcium disodium and trisodium ethylene diamine tetra-acetic acid in removing certain radioactive material from bone.

It was found that the calcium disodium salt appears nontoxic and has a considerable effect on the excretion of radioactive yttrium in both young and old animals if given shortly after the injection of the isotope. If given two weeks after the injection, it reduces the skeletal burden in young rabbits, but not appreciably in older animals. It is without effect on the excretion of radioactive strontium.

This chelating agent may well be of therapeutic value in persons who ingest certain bone-seeking isotopes.—*J. H. Harris, M.D.*

BRYANT, J. RAY, BERG, HAROLD F., and CHRISTOPHERSEN, WILLIAM M. Localization of radioactivity in the lung and the lymph nodes. *J. Thoracic Surg.*, Sept., 1953, *26*, 221–232.

The authors report on experimental methods of delivering effective radiation to specific segments of the lung and the regional lymph nodes.

In the first method, a colloidal solution of radioactive Au^{198}, containing 2 to 5 mc., was instilled through a catheter into a selected segment of a lung in 20 dogs. The dogs were sacrificed at varying intervals and assay for radioactivity showed a high concentration in the segment into which the solution had been instilled. High levels were also found in some of the regional lymph nodes. The longer the survival, the greater was the concentration of the radioactivity in the lymph nodes. Histological studies revealed necrosis of the treated lung segment, the necrosis being roughly proportional to the amount of the isotope instilled. Only minor histological changes were found in the lymph nodes.

In the second method, 2 mc. of a solution of radioactive colloidal Au^{198} was injected into the submucosa of the right intermediate bronchus of 8 dogs. In these, the radioactive concentration in all the hilar lymph nodes was consistently high. The site of injection showed less activity.

In both methods, the uptake in other organs, particularly the liver and spleen, was very low, indicating that little radioactive material entered the blood stream.

The possibility of human application was considered. If the radioactive dispersion in a segment of the lung involved with carcinoma and the uptake in the regional lymph nodes are high enough to deliver a therapeutic amount of radiation, a certain degree of palliation should be anticipated. Yet the dogs used were without tumor. In the event the

lymphatics are plugged with tumor, it is possible the radioactivity in the lymph nodes may not be as effective as desired.—*Paul C. Olfelt, M.D.*

Machanic, Harmon J., and Lieberman, Bernard. A new device for radiographic measurements. *Radiology*, Sept., 1953, *61*, 405–407.

Several methods for the accurate roentgenographic determination of object size, without resorting to precision stereoscopy, have been employed in the past. The authors present a novel method employing laminagraphy.

The measuring device, which is included in the plane of the laminagraphic cut, consists of copper or silver wires 15 cm. long, spaced 0.5 cm. apart, and imbedded in an easily obtainable thermal setting plastic. With this laminagraphic ruler placed as close to the part to be measured as possible, a cut is taken through the central point and 0.5 cm. above and below. This central point is determined in the usual way, by right angle roentgenograms or directly from body landmarks. Measurements are made directly from the ruler, which appears as a series of dots.

The authors have employed this method with success in determining the length of the femoral neck prior to hip nailing and other mensurations about the hip, but they suggest several other possible uses such as size and location of foreign bodies, pulmonary cavities, dimensions of medullary canal prior to insertion of intramedullary nails, and other situations where accurate measurement within the body is desirable.—*Michael J. Healy, M.D.*

Langreder, W., and Schüly, H. Zur Ausmessung von Skelettgrössen mittels direkter Massstabprojektion auf das Röntgenbild unter besonderer Berücksichtigung der Conjugata-vera-Messung. (Measurement of skeleton size by means of direct measuring stick on the roentgenogram with special emphasis on measuring the conjugata vera.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Oct., 1953, *79*, 511–519.

A simple direct method of roentgen measurement of skeleton size is presented. It is based on the idea that a certain number of centimeters is projected on the film under similar circumstances simultaneously with the object to be measured. Thus, the desired size on the film may be carried over and read directly on to the film object.

The authors use a plexiglass ruler marked off in centimeters with lead lines or dots. The ruler is placed parallel to the object to be roentgenographed and thus simultaneously projected on the film. A measuring plate may also be used, in which case a separate exposure is made of the plate and one for the patient. When the measuring ruler or plate is placed perpendicular to the central ray of the tube, there is no appreciable projection enlargement. The greater the focus-film distance in relation to the object-film distance, the more accurate is the measurement. Displacement of the measuring ruler should not exceed 2.0 cm. from the midline and the angle should not be greater than 10 to 15° from the parallel. An error greater than 3 mm. has not been encountered.

In measurement of the conjugata vera, the profile view offers an accurate procedure. The measuring ruler is placed high between the thighs and parallel to the bottom of the film. Thus, the ruler is at the same level as the conjugata vera and at the same distance from the film. No formulae or calculations need be used. The conjugata vera measurement may be read off directly from the ruler projected on the film. When using a focus-film distance of 100 cm. the margin of error is 3 mm. The pelvic inlet measurement is done with the measuring plate. A separate projection is made for the patient and one with the plate. The height of the symphysis is determined, when the roentgenogram of the patient is made, by taking into consideration the height at which the measuring plate is placed when the exposure is made for it. No corrections are necessary in measuring directly the pelvic inlet.—*Samuel Richman, M.D.*

Hellström, B. The reaction of the lung on bronchography with watersoluble contrast media in rats; comparison between two media. *Acta radiol.*, Oct., 1953, *40*, 371–382.

The reaction of the lung to two water-soluble media, umradil-viscous B (Astra) and ioduran B (Cilag) were compared by pathological studies of white rats following bronchography. No residues were found with the former throughout a six months follow-up period. With ioduran B, however, severe and irreversible changes occurred.

With these water-soluble media the iodized material itself is rapidly absorbed and can no longer be seen roentgenographically after a few hours. However, the viscous component (carboxymethyl cellulose), despite its water solubility, is not absorbed so readily. Its removal is effected by at least two mechanisms: it is eliminated from the bronchi by coughing and ciliary activity, and from the alveoli by phagocytes.

In the animals whose bronchial segments were injected with umbradil-viscous B the carboxymethyl cellulose is, on the whole, removed from the bronchioles and alveoli in forty-eight hours. One to six months after injection it may be found in absolutely minimal traces in occasional alveoli and phagocytes, but otherwise the histological picture of the lung is normal. In animals injected with ioduran B, on the other hand, in most cases severe changes were found

in a portion of the lobe into which the material had been injected. Forty-eight hours after injection carboxymethyl cellulose could be found, principally in distended bronchioles and alveolar ductules and the peripheral lung tissue was collapsed. This collapse persisted in the majority of cases and a chronic indurated pneumonic process developed.

The fact that ioduran B is about five times more viscous than umbradil-viscous B is felt to be an important cause for the difference in response.—*John F. Weigen, M.D.*

WANG, THEODORE J. Selective shielding against roentgen radiation. *Radiology*, Sept., 1953, *61*, 401–404.

Because of the frequent need for selective shielding in biological work, the author presents a study of the contribution of scatter from remote regions to the dose delivered at a particular point in a phantom.

A circular lead shield was mounted atop a presdwood phantom. By means of a Victoreen thimble ionization chamber, radiation intensities were measured in the center of the beam at 1.6 and 13.6 cm. Lead shields of various radii up to 9 cm. were employed. The incident radiation used was generated at 200 kv. p., and with a half-value layer of 1.0 mm. copper.

It was found that more than half the dose at 13.6 cm. resulted from side scatter arising from regions of the phantom at least 4 cm. removed, and about one-fourth of the dose resulted from radiation scattered at least 8 cm. For points which were closer to the surface of the phantom on the axis of the beam, the contribution from scattering was less. At 1.6 cm. depth, half the dose came from regions at least 1 cm. removed and one-fourth from distances over 3.5 cm.

A selective shielding sometimes employed with small animals is an encircling lead band about the region to be protected. The applicability of such a simple band technique is obviously limited in view of the foregoing considerations on scattering.—*Arthur R. Watson, M.D.*

HALE, ALFRED R., and BAILLIF, RALPH N. The retention and elimination of colloidal thorium dioxide in the albino rat following protracted administration. *Anat. Rec.*, Oct., 1953, *117*, 163–174.

The purposes of the study presented in this paper were (a) to measure the relative efficiencies of certain reticuloendothelial organs after protracted administration of thorium dioxide in colloidal form, and to compare the relative abilities of these organs to retain the salt following different routes of injection; (b) to test the possibility of reticuloendothelial blockage by associating this phenomenon with retention level; (c) to determine the routes of elimination, correlating these with the related "efficiency" of the reticuloendothelium of liver, lung and spleen.

Although considerable attention has been devoted to the study of the distribution of colloidal thorium dioxide, little has been done to associate dosage level with the relative efficiency of liver, spleen, omentum and lung for the segregation of large doses of thorium dioxide, or to compare relative powers for retention when the colloid is administered by different routes.

Of 106 female albino rats, 40 animals were chosen at random and of these 30 were injected intravenously with 3 cc. thorotrast every seventh day for 109 days, and 10 control animals received dextrin. Of 40 random animals in the second group, 30 were injected intraperitoneally with 0.5 cc. thorotrast each seventh day for 120 days, and 10 intraperitoneal controls were similarly injected with dextrin. The remaining 26 control animals were used for evaluating general colony status.

Shifts occurred in quantities of thorium retained by the liver and spleen, and losses of thorium from these organs were coincidental in time with increased uptake by the lungs.

Increased relative amounts of thorium excreted by the kidney were associated with apparent complete saturation of liver and spleen and it seemed that continued administration of the colloid introduced toxic effects which activated kidney excretion. Appearance of significant amounts of thorium in the feces was correlated with large accumulated amounts of the salt in the liver and also with increase in accumulation rate in the lung. Apparently excretion via the feces took place through the bile and possibly through swallowed secretions from the lung.—*John R. Smith, M.D.*

LUSTED, LEE, B., PICKERING, DONALD E., FISHER, DELBERT, and SMYTH, FRANCIS SCOTT. Growth and metabolism in normal and thyroid-ablated infant rhesus monkeys (macaca mulatta). V. Roentgenographic features of skeletal development in normal and thyroid-ablated infant rhesus monkeys (macaca mulatta). *A.M.A. Am. J. Dis. Child.*, Oct., 1953, *86*, 426–435.

The purpose of this paper, according to the authors, was to integrate roentgenologic features of skeletal growth and development in normal and athyroid infant rhesus monkeys with previously reported studies of growth and metabolism in the same animals. Skeletal growth and maturation were evaluated by serial roentgenograms.

They found that the role of thyroid in skeletal growth and maturation of normal and I^{131} thyroid-ablated (treated and/or untreated with l-thyroxine) infant rhesus monkeys, as evaluated by using serial (30 day) roentgenograms, was as follows: Linear bone growth was constant among normal infants and between 60 and 160 days increment of tibia or femur was approximately 20 mm. Skeletal maturation among normal infants was characterized by rapid ap-

pearance of secondary centers of ossification. Skeletal changes induced by thyroid ablation included marked and uniform diminishing rate of linear bone growth; delayed appearance of secondary centers of ossification; and skull changes characterized by an over-all growth deficit, enlargement of the sella turcica, delayed closure of sutures, delayed eruption of deciduous teeth, and flattening and thickening of the occipital bone with overriding by the basiocciput.

Adequate replacement therapy (20γ per kilogram per day of l-thyroxine) resulted in the resumption of a normal rate of linear bone growth, appearance of secondary centers, of ossification, and developmental progression toward normal skull features. Administration of 6γ per kilogram per day reversed all effects except those in the skeleton.—*R. S. Bromer, M.D.*

Mortimer, Robert K., and Tobias, Cornelius A. Evidence for x-ray induced recessive lethal mutations in yeast. *Science*, Oct. 30, 1953, *118*, 517–518.

The authors have attempted in their present experiment to show by another procedure the presence of roentgen-ray induced recessive lethal mutations in irradiated yeast. This was done by demonstrating a reduction in the percentage of germination of spores produced by diploid cells previously exposed to a small dose of roentgen rays. The sporulation of a diploid cell carrying recessive lethal mutations would bring about segregation of these mutations to the nuclei of the 4 haploid ascospores. Those spores receiving recessive lethal mutations would fail to germinate, and would thus provide a direct means of detecting this form of radiation-induced damage.

By using a special procedure and recording their data or results in table form, the authors show that the exposure of yeast cells to roentgen rays resulted in the induction of recessive lethal mutations and that in nearly every case, asci produced by the unirradiated diploid cells contained 4 viable spores. Asci arising from the irradiated diploid cells, however, exhibited a statistically significant reduction in the percentage of viable spores which they contain. This is considered indicative of segregation of lethal gene or chromosomal mutations. These mutations most likely were recessive since, at the doses used, the diploid cell that carried them would still have been viable for vegetative reproduction.

The authors conclude that the experiment demonstrates the presence of roentgen-ray induced recessive lethal mutations in yeast, but that it still does not prove that this is the only form of lethal damage induced. The extension of the radiobiological data on haploid and diploid yeast to triploid and tetraploid yeast cells indicates that some other form of lethal damage is also induced by the roentgen radiation. This damage has been proposed to be in the form of dominant lethal mutations.—*T. E. Padgett, M.D.*

Bennett, Leslie R., Chastain, Sarah M., Flint, Jerry, S., Hansen, Robert A., and Lewis, Alvin E. Late effects of roentgen irradiation. I. Studies on rats irradiated under anoxic anoxia. *Radiology*, Sept., 1953, *61*, 411–419.

In a previous study concerning the effects of anoxia on roentgen irradiation injury in rats it was found that irradiation under extreme anoxia shifted the LD 50 measured at thirty days from a little over 600 r to over 1,200 r. All those animals from the group irradiated with 1,000 r, 1,200 r, and 1,400 r which survived thirty days were kept and evaluated for the late irradiation effects. Only a few of the rats irradiated with 600 r and 800 r were kept and evaluated.

Clinical and postmortem observations indicate that there were three postirradiation periods: from the 30th to the 100th day, from the 100th to around 300 days, and from around 300 days to 540 days.

The late effects found were:

1. Marked shortening of the life span.
2. A high death rate due to pneumonia with a rather specific cell type in the granuloma.
3. Nephrosclerosis and generalized arteriosclerosis
4. Hypertension.
5. A blood dyscrasia characterized by thrombocytopenia and anemia.
6. Cataracts in the animals surviving ten months or more.
7. General cachexia.
8. Late epilation over head and neck.

A discussion of the possible mechanisms producing these late effects is presented.—*Donald N. Dysart, M.D.*

Stiennon, O. Arthur. "Punch-card" sorting for radiological reports. *Radiology*, May, 1953, *60*, 708–713.

It is generally agreed that a good coding and tabulating device for radiological reports is highly desirable. Such a system, having the advantages of low cost and minimal expenditure of time, is described.

The device consists essentially of marginal punch cards which may be sorted mechanically, and is apparently simple and efficient. For a detailed account of the way the system operates, the interested reader is referred to the original article.—*McClure Wilson, M.D.*

Zirkle, Raymond E., and Bloom, William. Irradiation of parts of individual cells. *Science*, May 8, 1953, *117*, 487–493.

The original of this paper should be read for an appreciation of the ingenious, meticulous procedure of the authors. Using 2 mev. protons from a Van de

Graaff electrostatic generator, with a range in tissue of approximately 73 microns, a microbeam was established by passing the emergent beam through one of two types of microapertures. One type was made by scratching with a diamond one jaw of an optically flat set of slit jaws. A similar type was made by "chopping" a jaw by means of a carefully controlled collision with an optically polished blade. The second type was formed by crossed slits, the jaws of which were polished to optical flatness. The first type of aperture provided essentially isodiametric cross-sections while narrow "ribbon" microbeams could be produced by the second type. For each microaperture, the energy spectrum of the protons incident on the cell was determined by measuring the lengths of the individual tracks produced on Ilford C2 plates after the protons had passed through mica of the same thickness as that used for the cover slips of the culture chambers.

Exact centering was obtained by an ingenious system of stops and controls, allowing a reproducible centering upon the desired area. It was possible to irradiate small portions of cells, even small portions of nuclei and occasionally a single chromosome. Previous techniques of irradiation have included large fractions (25–50 per cent) of cells or else the cells have been of exceptionally large size or possessed an eccentric nucleus. Prebombardment and postbombardment records were made by time-lapse photography.

The cells were grown in tissue cultures of amphibian heart (*Triturus*, *Ambystoma*). The experiments described were limited to mitotic cells. As a background for interpretation of the results of partial cell irradiation, 120 nonirradiated cells were observed and some 250 cells were totally roentgen irradiated with from 50 to 4,000 r. The disturbances noted following total cell irradiation were seen in the partially irradiated cells but were localized according to the spot of bombardment. Of particular interest was the fact that although even a few dozen protons to the chromosomes regularly produced unambiguous abnormalities (chiefly bridges), hundreds and even a few thousands to extrachromosomal regions (generally cytoplasm, spindle, centriolar region) produced no detectable effects, if no more than a few protons were scattered into the chromosomes.

As the authors state, this technique complements microsurgery. The method would seem applicable to many uses.—*T. J. Wachowski, M.D.*

WATROUS, R. M., HODGES, HAZEL W., and MCANDREW, M. J. Radiation burns from diffraction apparatus simulating infections; report of cases. *J.A.M.A.*, June 6, 1953, *152*, 513–514.

Roentgen-ray diffraction apparatus is commonly used in determining the molecular structure of many organic and inorganic compounds.

The authors point out the danger of roentgen burns unless proper operating precautions are followed. To illustrate, they report five radiation burns occurring in 3 persons over a period of two years. The diffraction apparatus described was in use at the Abbott Laboratories and in each case was improperly employed for fluoroscopy of fingers. Despite the characteristic appearance, delay in developing, and chronic course, the true diagnosis was not made until one of the patients suggested the possibility of a burn.—*R. E. Kinzer, M.D.*

CARLSON, J. GORDON, HARRINGTON, NYRA G., and GAULDEN, MARY ESTHER. Mitotic effects of prolonged irradiation with low-intensity gamma rays on the Chortophaga neuroblast. *Biol. Bull.*, June, 1953, *104*, 313–322.

The eggs of *Chortophaga viridifasciata* (grasshopper) were exposed to gamma irradiation from an activated cobalt-aluminum alloy in a special chamber. The mitotic activity was determined by counting the number of mid-mitotic neuroblasts from the first maxillary segment through the first abdominal segment at twenty-two minute intervals following cessation of the treatment. In the final experiment, the number of middle and later prophases were also recorded.

The authors found that when an intensity of 3.4 r per hour was used for six days, the mitotic count was reduced to about 40 per cent of normal for a period of seven hours following the treatment. The same dose given in a few minutes would have reduced the mid-mitotic count to zero for about five hours after the treatment.

Continuous irradiation with 0.8 r per hour failed to produce a significant mid-mitotic effect at the end of two days. A significant increase in the number of mid-mitoses was found at the end of four and also at the end of six days. This, however, was due to a simultaneous progression into mid-mitoses of neuroblasts that had accumulated in the late prophase as a result of the inhibiting effect of irradiation on this stage.

This study demonstrates again that irradiation can retard but not stimulate the mitotic progress of cells.—*Charles W. Cooley, M.D.*

NICHOLS, GREGORY B. An inexpensive semiautomatic serialographic apparatus for angiography. *J. Neurosurg.*, May, 1953, *10*, 323–326.

A home-made apparatus for multiple serial roentgenography in cerebral angiography is described. Detail drawings of its construction are presented. The apparatus uses standard 10×12 inch cassettes, requires only one technician to operate and permits exposures at one second intervals. It is useful only in

the lateral view. The cost is about $20.00 to $25.00.—*Joseph Levitin, M.D.*

Scott, Charles Waldo, Harper, Donald McCarthy, Jason, Robert S., and Helwig, Elson B. Neonatal granuloma venereum. *A.M.A. Am. J. Dis. Child.*, March, 1953, *85*, 308–315.

A case of neonatal granuloma venereum involving the right postauricular area, the right radius, umbilicus and penis in a five month old infant is reported in this article. As far as the authors can determine it is the first such reported case.

The roentgenogram of the right forearm showed destruction of a large part of the shaft of the radius by a central lesion with considerable periosteal reaction. The involved portion was fusiform in shape with a tendency to ray formation. Roentgen therapy was attempted as the differential diagnosis was thought to be either Ewing's tumor or tuberculosis. After each roentgen exposure an increase in size of the lesion occurred.

Finally the diagnosis of granuloma venereum was made and stibophen administered, this resulting in diminution of the lesion in the radius and eventual regression to a normal configuration.—*Ralph S. Bromer, M.D.*

Vogler, E., and Gollmann, G. Über angiographisch nachweisbare Gefässveränderungen bei Sklerodermia diffusa. (Vascular changes in diffuse scleroderma demonstrated by angiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1953, *78*, 329–335.

Scleroderma causes not only the well-known skin alterations, but also changes in other organs. The authors believe that these changes are due to vascular disturbances and, therefore, have done angiographic studies on hands and wrists of 6 patients (2 men and 4 women) to study them.

Technique: 10–20 cc. of water-soluble contrast medium (umbradil or ioduron) was injected into a brachial artery by the open route and 10–15 serial roentgenograms were taken in intervals of three seconds. Thorotrast was also used.

Results: Vascular changes corresponding to endangiitis obliterans were found routinely, most marked in the ulnar and less pronounced in the interosseous and radial arteries. The smaller vessels, particularly of the fingers, were also narrowed and only the artery of the proximal phalanx showed good filling. Occasionally, an arteriovenous shunt was noted in the arm.

The authors believe that the primary cause for these vascular changes and scleroderma as a whole lies centrally, probably in the hypophysis and the diencephalon. However, an additional factor (disposition) must also be present, explaining why some patients develop scleroderma and others Raynaud's disease.—*E. G. Wissing, M.D.*

Holmes, George W. Walter Bradford Cannon: 1871–1945. *Radiology*, July, 1953, *61*, 3–7.

Walter Bradford Cannon was born at Prairie du Chien, Wisconsin, October 19, 1871 and died in Franklin, New Hampshire, October 1, 1945. He came from early American French and Scotch-Irish stock. Dr. Cannon had his college and medical education at Harvard, graduating from college in 1896, summa cum laude. He supported himself and also had the aid of scholarships. Following his graduation from medical school he joined the faculty of Harvard and in 1906 became George Higginson Professor of Physiology, which post he held for the next thirty-six years.

Dr. Cannon's earliest research work was in the study of the movements of opaque media through the gastrointestinal tract, using the cat as his main test subject. Noting that fear stopped the motion of the stomach, he then began his investigations of the ductless glands.

During World War I, he entered the armed forces as First Lieutenant and at the time of his discharge he held the rank of Lieutenant Colonel. In this period he did a great deal of investigation on shock. He received many honors in recognition of it. In 1939 Dr. Cannon became President of the American Association for the Advancement of Science. His writings are seen in ten books in which he was author or co-author and over two hundred scientific papers.

Dr. Cannon strongly advocated a broad knowledge, not only in the researcher's own field but also in related fields. He advocated that the productive scholar have the following traits: curiosity, imaginative insight, critical judgment, thorough honesty, patience, good health, and generosity.

In 1931, Dr. Cannon developed a very pruritic case of mycosis fungoides. By 1938 this had progressed into a leukemic phase and caused his death in 1945. His symptoms were partially controlled by palliative radiation therapy. His early fluoroscopic work lead to the development of extensive keratotic lesions of his hands and forearms; one of these on his wrist developed into a carcinoma. Dr. Cannon was a tireless, determined and brilliant worker.—*Dean Nichols, M.D.*

Steinbach, Howard L., and Lusted, Lee B. A device to support patients during upright fluoroscopic examinations. *Radiology*, July, 1953, *61*, 80–81.

A simple sling type of device for supporting unsteady and poorly cooperating patients during upright fluoroscopy is presented. A band is passed

across the chest, under the arms, and is attached to the top of the table by a hook. This may also be used to support pediatric immobilization boards.—*William A. Goodrich, Jr., M.D.*

Rigler, Leo G., and Watson, John C. A rapid film-changing device for general radiography; preliminary report. *Radiology*, July, 1953, *61*, 77–79.

The many and varied devices at present available for the rapid changing of films or cassettes for special roentgen diagnostic procedures are not entirely suitable for several reasons. First, the roll film used in these devices is made only in one size, and hence not practical for general conventional roentgenography. Secondly, it is difficult to interrupt the roll before it is entirely exposed.

The authors describe and list the many advantages of a new apparatus, the engineering model of which is now being tested experimentally. The unit utilizes roll film which is advanced through a pair of intensifying screens at a maximum of five films per second. As each succeeding film is advanced into the exposure area, the previously exposed film is cut off by a motor driven knife. It is then transported to a receiving magazine where it can be removed and processed at any time. The unit is constructed to fit the conventional roentgenographic table or stereoscopic cassette changer. Its design is such as to permit its substitution for conventional cassettes and intensifying screens in many types of roentgenography.

The model is at present being tested under standard operating conditions in a large department of radiology in order to determine its practical usefulness for conventional roentgenography.—*Michael J. Healy, M.D.*

Fineman, Sol. A simple device for saving films in radiography of the intestine. *Radiology*, July, 1953, *61*, 71–76.

The author has designed a special abdominal binder for use in obese patients during roentgenographic examination of the colon and small intestine. Rectangular rubber compression bladders in the abdominal binder are inflated to compress the patient's flanks. This makes it possible to depict the entire large and small intestine on a single 14×17 inch film placed lengthwise under the patient.—*Arno W. Sommer, M.D.*

Eisenreich, Franz X. Untersuchungen über die Entstehung von Lungenatelektasen bei Ausschaltung der Lungennerven und unter anderen Bedingungen. (Investigations on the mechanism of atelectasis with interruption of lung nerves and under other conditions.) *Thoraxchirurgie*, Aug., 1953, *1*, 262–280.

The author describes various animal experiments which show that neuromuscular theories of atelectasis can be ruled out.

In the clinical part of the paper the following types of atelectasis are discussed: (1) atelectasis during surgery when the thorax is open, (2) postoperative atelectasis, and (3) plate-like atelectasis.

The first two types occur when ventilation of the lung is prevented while the blood supply remains intact. Other reasons mentioned are mechanical pressure on a lung segment by a surgical instrument or by a rib and kinking of a bronchus. Three cases are presented as examples of postoperative atelectasis. One had a large mucous plug, the others a great deal of pus and secretion with pressure of enlarged lymph nodes on a main bronchus causing occlusion of bronchi. Other complicating factors are aspiration of secretions during anesthesia, abnormally increased bronchial secretion by an irritated or diseased bronchial mucosa (chronic bronchitis, asthma), irritation of the bronchial mucosa by the anesthetic agent, diminished cough reflex and favoring of the operated side due to pain.

Plate-like atelectasis is observed during the process of resolution of massive atelectasis and is due to uneven aeration. The atelectasis seen with paralysis of the diaphragm and the basal atelectasis of the aged are attributed to compression of the lungs by the elevated diaphragm.

The treatment is discussed briefly.—*Frederick M. Reis, M.D.*

Loiseleur, J. L'intervention de l'oxygene en radiobiologie. (The rôle of oxygen in radiobiology.) *Ann. Inst. Pasteur*, June, 1953, *84*, 1601–1609.

The author has pursued for the past twelve years a series of experiments which tend to demonstrate that the effects of irradiation are due to the primary radioactivation of the molecular oxygen found in solution in the irradiated tissues. An initial experiment showed that the irradiation of a solution of quinhydrone in the presence of oxygen resulted in oxidation and its transformation into quinone. In general, all irradiation which takes place in the presence of oxygen results in oxidizing effect: benzidine, pyrogallol, adrenalin and other substances develop evident photocolorimetric reactions but only when the irradiation is done in the presence of oxygen; the same is true of irradiation of organic acids, aldehydes and alcohols in aqueous solutions. The irradiation of amino acids results in their transformation into per-acids even when they are irradiated as part of the protein molecule. The irradiation of tetanus toxin and of strychnine results in a diminution of their toxic effect comparable to a dilution; the toxicity of strychnine is unchanged if the irradiation is carried out in the presence of an oxygen-avid substance, such as ferrous sulphate.

A practical application of these findings would be

the possibility of artificially increasing and decreasing natural radiosensitivity: the experimental hyperglycemic rabbit shows a lessening of skin radiosensitivity as compared with that of controls; conversely a hypoglycemic rabbit shows an increase of skin radiosensitivity.

The irradiation of a solution of tyrosine has shown interesting "latent" effects: the resulting changes in color of the solution progress for several days after irradiation, as though the peroxide which results from irradiation continued to have its effects. This latest experiment suggests the possibility of counteracting the untoward effects of an accidental irradiation, or those resulting from atomic warfare, by the administration of reductor substances to neutralize the peroxides before this may have acted upon the cellular elements.—*J. A. del Regato, M.D.*

DE SOUSA, AYRES. Cavoquimografía. (Cavokymography.) *Acta iber. radiol. cancerol.*, April-June, 1953, *2*, 145–162.

One of the most interesting features found in angiokymographic practice, as observed by the author, is without doubt the phenomenon of segmentation. When a contrast substance is injected into an artery at a constant rate and a roentgen kymogram is made, a clearly segmented tracing is obtained. Studies were first made experimentally with the conditions in which segmentation appears, with the observation that it resulted from greater or lesser dilution of the opaque medium in the blood. The angiokymograms made of the aorta of the rabbit suggest a definite relationship to the velocity curves known from physiology. As the velocity of the blood in the vessel increases as a result of cardiac systole, the opaque liquid which is introduced at a constant rate suffers a greater dilution at the moment, and consequently causes the appearance of a less opaque segment in the kymogram. The opposite phenomenon appears during diastole, occasioning a more opaque segment; and the result of this rhythmic sequence is the segmented aspect of the arteriokymogram.

It seemed reasonable to seek the explanation of the above finding in the physiologic bases of the venous pulse. The dense segments of the phlebokymograms correspond to the positive phase of the venous pulse through slowing down of the blood flow in the vena cava and the consequent greater concentration of the opaque medium. On the other hand, the less dense segments correspond to the phases of venous collapse, both systolic and diastolic when the blood flows more quickly in the vena cava and the concentration of the contrast substance is diminished. Systolic collapse of the vein is interrupted only by the positive wave *c* which is not registered in the cavokymograms, a fact attributable to the short duration of this positive wave (only 0.153–0.2 second) and to the partial superimposition of the *a* wave. With a rapid film it is possible that its presence could be registered in the angiokymographic tracings.

The advantages of this method lie in the possibility of studying any point of the superior vena cava, inferior vena cava, or even the peripheral trunks. The cavokymogram would be the true central venous pulse, a term generally reserved for the tracings of the jugular vein, since it is recognized that at that level all the hemodynamic oscillations in the central venous trunks are felt.

Because the cavokymogram is the direct graphic record of a pencil of rays passing through the slit of the kymograph, it is not necessary to reckon with the inertia of the mechanical systems which sometimes give rise to discordance in the results, as in the phono- and phlebograms.

The object of this study was not to arrive at definite conclusions on any particular problem in physiology or physiopathology but only to show the possibilities of angiokymography in some of the problems of hemodynamics and to point out the increasing importance of roentgenology in future investigations upon the circulation.—*James T. Case, M.D.*

HODGES, PAUL C., JR. Ossification in the fetal pig; a radiographic study. *Anat. Rec.*, July, 1953, *116*, 315–325.

The author has studied the roentgen findings in the skeletal development of 330 pigs (63 litters), measuring 25 mm. to 290 mm. crown-rump length, impregnated with silver nitrate.

The fresh fetuses were fixed for forty-eight hours in 95 per cent alcohol, and then put into a solution of 0.5 per cent silver nitrate.

It was noted that fetal length at best is an approximate indication of fetal age.

From this study it was observed that the fetal length varied considerably at the time when an ossification center appeared and the length at which it was invariably present. In the humerus and femur the variation in length was only 4 or 5 mm., but in the tympanic part of the temporal bone the variation was 30 or 40 mm.

There are many similarities and many differences between the ossification patterns observed in the pig and those accepted as normal for man.—*John Watts, M.D.*

EPPRECHT, W., ROSENMUND, H., and SCHINZ, H. R. Chemische, mineralogische und Röntgen-Feinstrukturuntersuchungen an Gallensteinen des Menschen und des Rindes. (Chemical, mineralogical and roentgen diffraction studies of human and bovine gallstones.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, July, 1953, *79*, 1–20.

Sixty human and twenty-two bovine gallstones were studied with mineralogical, chemical, routine

roentgenographic and roentgen diffraction methods.

Most of the human stones consist of copper-calcium bilirubinates or calcium bilirubinate or of cholesterol. These constituents are either thoroughly mixed in the stone or they are separated in core and rind. Proteins, apatite, vaterite and calcite are also found to a lesser degree. Bovine gallstones consist mostly of calcium bilirubinate, both amorphous and crystalline.

The authors propose a new classification of gallstones based upon their constituents. Group A comprises homogeneous and Group B heterogeneous stones. The former are subdivided into cholesterol stones and bilirubinate stones and the latter into mixed stones and combined stones.—*Otto Glasser, Ph.D.*

Bowers, J. Z., Davenport, V., Christensen, N., and Goodner, C. J. Effects of acute whole-body x-irradiation on salt and water metabolism and their clincial significance. *Radiology*, July, 1953, *61*, 97–102.

As a part of a series of physiologic and pathologic investigations into the effects of the acute radiation syndrome, a group of rats were given whole body irradiation. The rats were held in immobilization devices allowing separate collections of urine and feces. An LD_{50} dose of 660 r, with factors of 250 kv., 15 ma., and 0.5 mm. Cu and 1 mm. Al filtration was administered. A similar group acted as controls and were pair-fed from a stock diet. Six treated and 6 control animals were used for each test period, lasting 24, 96, and 240 hours after irradiation. After sacrifice at the ends of these periods, tissue from skeletal muscle, liver, and small intestine were analyzed. Amounts of sodium, potassium, and chloride were determined. Corrections were introduced by determinations of fat, blood plasma, and drying of tissues.

Soon after irradiation there was a diminished food intake with a concomitant negative balance of the three electrolytes. No significant changes in plasma potassium levels and only minor deviations in plasma sodium were observed. This is probably due to the ability of the kidney to maintain a proper balance.

The small intestine showed an increase in sodium and chloride and a decrease in potassium at twenty-four hours, but the electrolyte levels were normal at ninety-six hours. Liver samples showed an increase in potassium at twenty-four hours. Though the findings are not conclusive, they indicate that a radiosensitive tissue such as the small intestine loses its ability to maintain concentration differences between extracellular and intracellular fluids due to an interference with cellular metabolism. Restoration of normal metabolism appears to occur rapidly (*viz.*, 96 hours).

In the acute radiation syndrome gastrointestinal ulceration, diarrhea and vomiting, with resulting decreased absorption and loss of electrolytes will complicate the electrolyte in balance in addition to this strictly cellular disturbance. Treatment of the acute radiation syndrome must include attention to potassium and nitrogen replacement as well as parenteral feedings, including protein derivatives. Frequent determinations of the serum potassium, sodium, and chloride, with cognizance of the place of kidney function in maintaining or altering these levels, should aid materially in the management of the radiation syndrome.—*William A. Goodrich, Jr., M.D.*

Rossi, Harald H. The *n* unit and energy absorption in tissue. *Radiology*, July, 1953, *61*, 93–96.

The *n* unit represents the quantity of neutron radiation that will produce the same ionization in a 100 r Victoreen chamber as 1 roentgen of x-radiation. Since it was introduced by Aebersold and Lawrence in 1942, the *n* unit has been used extensively to quantitate neutron exposures of biological material, although it suffers from a number of limitations. The unit is arbitrary in the sense that the factor relating the response of the ionization chamber to energy absorbed in tissue depends on several complex variables. Another difficulty arises from the fact that Victoreen chambers are not designed for the measurement of fast neutrons.

Studies were undertaken by the author to obtain further information on the energy absorbed by tissue exposed to 1 *n* of fast neutrons and on the likely limits of variation of this quantity caused by inherent differences between Victoreen chambers. Four sets of Victoreen chambers, each set consisting of a 25 r and a 100 r chamber, were calibrated to obtain the absolute roentgen-ray sensitivity of all chambers. One of the neutron sources was the beryllium target of a 33 inch cyclotron. The other source emitted fast neutrons with a spectrum characteristic of fission of U^{235}.

The response of Victoreen chambers to neutron radiation varies because of two factors: (1) The roentgen-ray response of chambers can differ, and (2) there is an intrinsic difference in neutron sensitivity which is in the order of 15 per cent. The average response of all 25 r chambers in all measurements was found to be 1.95 rep/*n*., while the corresponding figure for the 100 r chamber was 1.92 rep/*n*. It is concluded that the *n* unit is energy-independent over a range of neutron energies.—*Arno W. Sommer, M.D.*

Erlacher, Philipp. Zur Behandlung des Morbus Bechterew mit Thorium X. (The treatment of morbus Bechterew with thorium X.) *Wien. klin. Wchnschr.*, Sept. 25, 1953, *65*, 825–826.

Bechterew's disease (ankylosing spondylitis), de-

scribed by him in 1892, then by Strümpell in 1897 and by Pierre Marie in 1898, occurs more often in men than in women; some statistics give the ratio as 5:1. As far back as 1912 Bickel reported good results from the oral administration of thorium X.

More recently Pitzen undertook an experimental study on rabbits regarding any deleterious effect of thorium X. This agent apparently attacks young bone producing delay in growth, closing of the epiphyses and healing of fractures. Thirty-two patients treated by intravenous injection of thorium X and followed for periods of from ten to thirty years, did not show any ill effects referable to the treatment. The same author has treated so far approximately 200 patients by intravenous injection of 200 e.s.u. each given weekly for a total of 10 to 12 injections. It is important to watch the white blood cell count and stop treatment when it drops under 4,000. Of the first 120 cases treated from 1948 to 1950, 57 became asymptomatic, 56 were considerably improved, 6 were improved and 1 did not respond. Of these 120 patients 80 were re-examined a year later. At that time 60 were free from symptoms, 18 considerably improved and only 2 had not responded.

The author himself has treated so far 14 patients, 10 men and 4 women, strictly adhering to the technique of Pitzen. Four of these became asymptomatic, 5 were considerably improved, while 4 cannot yet be evaluated. The most impressive result of the treatment was the relief of pain.—*E. A. Pohle, M.D.*

Wood, Ernest H. Preliminary observations regarding value of a very fine focus tube in radiologic diagnosis. *Radiology*, Sept., 1953, *61*, 382–390.

Films of exceptional diagnostic quality, even with image magnification, can be obtained by using a tube with a small focal spot. In this study, a tube with a focal spot of 0.3 mm. was used, and its practical value is presented.

Experience has shown that image magnification of 2× preserves good detail when a 0.3 mm. focal spot is employed and the resultant enlargement aids at times in the diagnosis of fractures (particularly of the carpal navicular, femoral neck, and arches of the vertebrae), and diseases of the teeth, skull, lungs, bones, joints, mastoids, and paranasal sinuses.

A double sized image may be easily obtained by placing the focal spot 24 inches above and the film 24 inches below the object. The quantity of radiation, measured in milliampere seconds is slightly greater than in ordinary roentgenography because of the increased target film distance. Thorough immobilization and reduction of scatter radiation are of great importance. Stereoscopic pairs of these enlargements as well as excellent laminagrams can easily be made.

The teaching value of enlarged roentgenograms is worthy of further investigation.—*Arthur R. Watson, M.D.*

Boreadis, Anthony G. Upright cholangiography; a new device for simplifying cholangiography. *Radiology*, Aug., 1954, *63*, 226–229.

A specially equipped syringe to facilitate injection during cholangiography is described. With the patient in upright position, the T-tube is aspirated and under fluoroscopic observations 2.0 to 4.0 cc. of opaque medium is injected through the syringe. Spot films are then made in upright, recumbent and Trendelenburg positions.

The technique enables one to make fluoroscopic observations and take spot films in any position. The entrance of air bubbles into the system is prevented and better visualization of the common duct is claimed.

Ten figures demonstrate the improved roentgenographic results with this apparatus and technique.—*E. E. Seedorf, M.D.*

Devik, Finn. Protective effects of combined hypoxia and cysteine treatment on whole-body irradiation of mice. *Brit. J. Radiol.*, Aug., 1954, *27*, 463–466.

The author has made experimental studies of the protective effects of hypoxia and cysteine treatment on whole body irradiation of mice.

Both L-cysteine and D-cysteine were used, and no difference was found between their protective effects. In these experiments hypoxia was induced by leading a gas mixture of 8.45 per cent O_2 in nitrogen into a box in which the mice were kept during irradiation.

The mice were exposed to irradiation from 200 r to 1,100 r at 170 to 190 kv. The frequency of chromosome injuries in the bone marrow and the acute lethality were used to indicate the protective effects of buffered cysteine and hypoxia.

Cysteine and hypoxia were used separately and also in combination. The protective effect of the two was found to be additive, both as regards the lethal effect and the chromosome injuries.

The author believes that cysteine exerts its protective effect by a radiochemical rather than a biochemical action.—*D. V. Campbell, M.D.*

Jacobson, Leon O. Modification of radiation injury. *Bull. New York Acad. Med.*, Sept., 1954, *30*, 675–692.

It has been shown that a number of agents, when administered to certain mammals before or during the exposure of the mammal to whole body roentgen radiation in the lethal range, produce a beneficial effect upon the organism by increasing its chances of survival. In general, these agents do not

have any beneficial effect upon survival when administered after the animals have been subjected to lethal whole body irradiation.

This paper is a report on measures that, when initiated after exposure of the mammal to an LD 100, have a remarkable effect on survival and on recovery of the blood-forming tissue. It was found, during some experiments on the effects of radiostrontium in mice, that the animals did not develop anemia although their bone marrow became completely aplastic within a few days after injection and remained so for more than a month. Since strontium is almost exclusively a bone seeker, the spleen was essentially unaffected by it. This gave impetus to various spleen-shielding experiments. In these it was found that shielding the spleen during whole body irradiation gave a much higher percentage of survivals than in mice in which the spleen was not shielded. Intensive blood formation, beginning at the twenty-four hour interval, was observed in the shielded spleens of the heavily irradiated animals. Shielding of other parts of the body of the mouse was found to increase survival, but less so than spleen shielding, even though the volume shielded in each instance was much greater. Splenectomies were performed at intervals, beginning at fifteen minutes after irradiation with spleen shielding. As short a period as fifteen minutes was sufficient to increase survival. When the spleen was not removed until one hour after exposure, the survival rate (78 per cent) was comparable with that of the mice given routine spleen-shielding without splenectomy.

These findings led to experiments with spleen implants, after lethal whole body irradiation with no shielding of the spleen of the irradiated animal. Spleens of baby mice implanted intraperitoneally resulted in 38 per cent survival. Use of adult spleen implants failed to give protection. There were no survivals among the control animals which did not receive spleen implants.

Next, injections of embryo and splenic tissue suspensions were tried. The injections of embryo suspensions resulted in 30 per cent survivals. Splenic tissue suspensions did not give protection, but cells extracted from the spleen did produce a high survival rate. The efficacy of bone marrow in increasing the survival of irradiated mice was first reported by Lorenz, and was corroborated in this series of experiments. A number of attempts were made to obtain a cell-free extract of spleen, embryo or bone marrow that would increase the survival of irradiated mice, but with negative results. A pronounced difference in the species response was found. Spleen-shielding in the rabbit, for example, produced a definite but minimal effect. Some strain differences were also found, but these were not great. Antibody response to an injected antigen is inhibited by total body irradiation, but spleen shielding protects this function. In fact, the antibody response is retained when the shielded spleen is removed twenty-four hours after the total body irradiation, and the antigen is given forty-eight hours after the exposure (24 hours after splenectomy).

It has long been assumed that irradiation produces a toxin that has an inhibitory effect on metabolic processes within the irradiated cells, and that this "toxin" is transported to other parts of the body and is presumed to inhibit cellular processes at distant nonirradiated sites. If this is true, one must assume that the production and dissemination of the substance and the initiation of the biological effects occur within a relatively short time after irradiation, and that the "toxin" is then destroyed or neutralized. The spleen-shielding experiments seem to support this theory. It would appear that the effect produced by lethal irradiation represents a chain of events initiated by an agent such as hydrogen peroxide, and that the profound effect of spleen-shielding, or injection of such materials as embryonic tissue, spleen or bone marrow cells and the like could best be explained by assuming that these cells or tissues provide one or more of the metabolites necessary for the functional reconstitution of the injured cells.—*D. S. Kellogg, M.D.*

Barrett, Charles M. Radiation hazards in the practice of radiology. *Radiology*, Sept., 1954, *63*, 400–406.

Attention is called to the existence of radiation hazards encountered in the routine practice of radiology. Of the utmost importance is the fact that these existing dangers be recognized and that underlying physical principles be understood in order that these dangers may be minimized.

The scattered secondary rays are the main source of danger in diagnostic roentgenology. During fluoroscopy, protective gloves, aprons and other protective devices decrease the scattered radiation from the patient's body. Proper installation of equipment, along with its proper use, and routine check-ups will cut down the hazard.

Radium is potentially dangerous as a source of overexposure during loading of applicators or during actual implantation into the body. In the event radium is lost from its capsule, the long-lived alpha emitting isotopes, if ingested, inhaled or otherwise absorbed by the body, can cause much damage. Methods of finding, tracking down and removing this contamination are discussed.

In the field of roentgen therapy, the dangers are less because personnel are usually well removed and protected from the radiation. Proper shielding of the working area is the best solution to this potential danger.

The longer the half-life, the greater is the hazard when working with radioactive isotopes. The danger is much less when personnel are cognizant of the

problem of preventing radiation damage and contamination.

In conclusion the author states that the individual engaged in the practice of radiology should constantly review his technique and take the necessary steps to prevent injury to himself and his co-workers. —*Donald N. Dysart, M.D.*

Quimby, Edith H., Castro, Victoria, and Soifer, Charles. Dosage determination for rotation therapy in the horizontal plane. *Radiology*, Aug., 1954, *63*, 201–19.

In moving-field roentgen therapy when the patient is rotated about an axis at an angle to the beam, or the beam describes a circular path over one surface of the patient, the technique is called "horizontal" or "short-axis" rotation therapy. This technique is useful for lesions relatively close to one surface of the body, but is usually suitable only for spherical or relatively flat lesions.

The procedure involves use of a wax cone placed above the skin in such a manner that the end of the treatment cone just skims around the wax cone surface during rotation. By using a 45° wedge filter the inequality of dosage can be eliminated. Radiation with a half-value layer of 1.8 mm. Cu and a 50 cm. skin-target distance is used. The beam enters the surface at a 45° tilt with the radius of the skin path depending on the depth of the lesion. Depth dose measurements were made in a unit density presdwood phantom and isodose charts in four planes at 0°, 30°, 60°, and 90° to the plane in which the wedge exerted its greatest effort were constructed.

Since the dosage determination from these curves involves arduous calculation, the authors developed a procedure for determining approximate doses which would enable one to estimate easily whether this technique of therapy would be applicable in a specific case. Their procedure involves construction of a cross-section diagram in actual size, indicating exact positions of tumor, skin, beam and beam axis, and axis of rotation. On this diagram is placed the appropriate isodose chart—the one used depending on whether or not a wedge filter is employed and on the tilt of the beam—and the tissue dose read for each desired point. These isodose charts are constructed in roentgens at any point per 100 roentgens in air at the end of the treatment cone, without the wedge.

The values obtained by this approximate calculation method show good agreement with those obtained by the rigorous calculation method and by measured values.

In Appendix I the construction of a wedge filter is shown. Appendix II shows the construction of the wax cone. The method of calculating the average dose rates at a point according to Green, Jennings and Bush is shown in Appendix III.—*Donald N. Dysart, M.D.*

Robbins, Robert, and Meszaros, Jean. The calculation of rotation therapy tumor doses at 250 kv. by means of the transmitted dose rate. *Radiology*, Sept., 1954, *63*, 381–389.

A method of dosage determination in rotation therapy by the measurement of the dose rate of the transmitted radiation as a measure of the tissue dose at the axis of rotation is discussed. Measurements were made simultaneously of axis and transit dose rates in air and at the center of a series of water phantoms of various sizes and shapes. Factors were: 250 kv., half-value layer of 1.7 mm. Cu and target-axis distance of 85 cm.

These rotation therapy dose rate curves, if made at the time of each treatment by a rate-reading device, could be used as a method of re-positioning the patient during treatment to ensure proper beam direction. Other advantages of this transit method are that it permits recognition of day-to-day variations in tumor dose and that it shows changes in roentgen tube output. Horizontal rotation therapy techniques can also use this method for dosage determinations.

The major disadvantage of the method is that it gives information about dose at one point only—the axis. Off axis points and dose distribution studies still require dose plotting by the sector method.

Theoretical equations have been written for the transit dose, tumor dose, and for the axis eccentricity correction factor giving results which are in satisfactory agreement with the experimental values for all but the largest phantom area and eccentricity. The authors feel that when the instrument is further improved in order to meet the conditions imposed by the equations, experimental verification will not be a prerequisite to the use of these curves in other institutions.—*Donald N. Dysart, M.D.*

Walstam, Rune. The dosage distribution in the pelvis in radium treatment of carcinoma of the cervix. *Acta radiol.*, Sept., 1954, *42*, 237–250.

A series of isodose measurements were made in a water phantom around intrauterine and vaginal radium irradiators of varying types. Following Heyman's original recommendation of increased intrauterine irradiation, the author devised an irradiator of increased diameter containing up to seven short (10 mm.), 50 mg. tubes of radium. Thus from a 150, 250, or 350 mg. radium source placed well beyond the external os in a uterus centered within the pelvis, one may obtain increased irradiation of the lymph node regions. If the dose from the vagi-

nal irradiator is correspondingly decreased then the risk of overdosage to the rectum and bladder is obviated.

A description is also made of an instrument used clinically for one year for systematic dosage measurements in the urinary bladder and rectum of patients treated by the Stockholm method. The instrument utilizes a small graduated measuring probe with a minute ionization chamber at the end.

Eight figures are included showing dose distribution under various physical conditions.—*Arch H. Hall, M.D.*